# BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATON OF SHORT PHYSICAL ACTIVITY SESSIONS VERSUS A CONTINUOUS PHYSICAL ACTIVITY SESSION IN PREHYPERTENSION

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I would like to dedicate this dissertation to my parents, Mrs. YoungHee Ha, and Mr. YoungTae Park, who believed in and supported me.

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Saejong Park

# BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATON OF SHORT PHYSICAL ACTIVITY SESSIONS VERSUS A CONTINUOUS PHYSICAL ACTIVITY SESSION IN PREHYPERTENSION

Despite limited research, the accumulation of physical activity has been recommended for the treatment of prehypertension. The purpose of this study was 1) to compare the duration and magnitude of blood pressure (BP) reduction following the accumulation of physical activity ($PA_{accum}$) vs. a single continuous physical activity session ($PA_{cont}$), 2) to investigate the BP response during the rest periods between short sessions within the $PA_{accum}$, and 3) to investigate sympathetic modulation (SM) as a possible mechanism for BP reduction in prehypertension. Procedures include 1) BP screening, 2) maximal graded exercise test, 3) treatments ($PA_{accum}$, 4x10-min walk at 50% $VO_2$peak; $PA_{cont}$, 40-min walk at 50% $VO_2$peak; and control), and 4) 12-hr ambulatory BP, and SM measurements via heart rate variability. In this randomized within-subjects design, 20 prehypertensive completed the study. Systolic (S) BP was reduced -5.4$\pm$1.7 mm Hg for 11 hrs following $PA_{accum}$ and -5.6$\pm$1.6 mmHg for 7 hrs following $PA_{cont}$. Diastolic (D) BP was reduced -3.4$\pm$1.3 mmHg for 10 hrs following $PA_{accum}$ and -3.1$\pm$1.3 mmHg for 7 hrs following $PA_{cont}$. In $PA_{accum}$, the change in sympathetic modulation was correlated with both SBP and DBP reductions. In $PA_{cont}$, the change in sympathetic modulation was correlated with

DBP reduction. SBP was decreased following the third short session within the $PA_{accum}$ compared to the baseline. No significance was found in either DBP or SM during the rest periods between short sessions. In conclusion, the accumulation of PA appears more effective than a continuous session in the management of prehypertension. There is an additive effect of successive short sessions within the accumulation of physical activity on blood pressure reduction. Sympathetic modulation was associated with BP reduction following each PA treatment.

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***THE ACCUMULATION OF PHYSICAL ACTIVITY LEADS TO A GREATER BLOOD PRESSURE REDUCTION THAN A SINGLE CONTINUOUS SESSION IN PREHYPERTENSION***

**Short title:** Accumulation of physical activity

***ABSTRACT***

***Objectives*** Despite limited research, the accumulation of physical activity ($PA_{accum}$) has been recommended for the treatment of prehypertension. The purpose of this study was 1) to compare the duration and magnitude of blood pressure (BP) reduction following $PA_{accum}$ vs. a single continuous physical activity session ($PA_{cont}$), and 2) to investigate sympathetic modulation as a possible mechanism for BP reduction following each acute session.

***Methods*** Adults with prehypertension (n=20) completed in a randomized cross-over design. Ambulatory BP and heart rate variability (HRV; via Holter monitoring) were measured for 12 hrs following: a) $PA_{accum}$ (4x10-min walks (one/hr for 4 hrs) at 50% of $VO_2$peak), b) $PA_{cont}$ (40-min walk at 50% of $VO_2$peak), and c) control treatments. BP and HRV following each activity treatment were compared with the respective periods from the control treatment. HRV was correlated with BP reduction.

***Results*** Systolic (S) BP was reduced for 11 hrs following $PA_{accum}$ ($P<0.01$) versus for 7 hrs following $PA_{cont}$ ($P<0.05$). Diastolic (D) BP was reduced for 10 hrs following $PA_{accum}$ ($P<0.05$) versus for 7 hrs following $PA_{cont}$ ($P<0.05$). In $PA_{accum}$, the changes in normalized low ($r=0.517$, $P<0.01$) and high frequency ($r=-0.503$, $P<0.05$) power were correlated with SBP reduction and the changes in normalized low ($r=0.745$, $P<0.001$) and high frequency ($r=-0.738$, $P<0.001$) power, and changes in low:high frequency ratio ($r=0.756$, $P<0.001$) were correlated with DBP reduction. In $PA_{cont}$, the difference in low:high frequency ratio ($r=0.543$, $P<0.05$) was correlated with DBP reduction.

***Conclusion*** The accumulation of PA appears more effective than a single continuous session in the management of prehypertension. Sympathetic modulation was associated with BP reduction following each physical activity session.

**Key Words:** Ambulatory Blood Pressure, Post-exercise Hypotension, Fractionization of Exercise, Heart Rate Variability

## *INTRODUCTION*

In 2003, 45 million adults with prehypertension were added to the patient population in need of treatment for high blood pressure [1]. Lifestyle modification [1, 2], including regular exercise and/or physical activity, is the only recommended treatment for prehypertension. Lifestyle modification is also the only recommended treatment for the prevention of prehypertension progressing to hypertension [3]. Regular exercise and/or physical activity is considered to be one of the most promising lifestyle modifications for the treatment of hypertension [4]. Yet, research on exercise and/or physical activity as a treatment for prehypertension is incomplete [5].

Scientific evidence supports the effectiveness of regular exercise in the treatment of hypertension [6-8]. More recently, however, the accumulation of at least 30 minutes of moderate intensity physical activity on most, if not all days of the week has been recommended as the new “exercise” guidelines for both prehypertension and hypertension [1, 2]. Yet, the evidence on the effectiveness of physical activity on blood pressure reduction has come from studies investigating continuous exercise sessions [1, 2, 9] rather than from the study of the accumulation of physical activity. The limited scientific evidence supporting a recommendation of the accumulation of physical activity as a treatment for prehypertension precipitated our recent work in the physical activity treatment of prehypertension and hypertension [10].

Previously, we [10] investigated the effects of the accumulation of one day of lifestyle physical activity in prehypertension and hypertension. The

accumulation one day of lifestyle physical activity over a 12-hour period was found to reduce systolic blood pressure in adults with prehypertension (6.6 ± 2.3 mmHg for 6 hours) and hypertension (12.9 ± 4.3 mmHg for 8 hours). The results of our study were noteworthy for the treatment of both prehypertension and hypertension. However, the restraints of this field study were 1) the participants accumulated 4-6 hours of lifestyle physical activity, which is well beyond the recommendations [1, 2]; 2) the types of lifestyle physical activity were not controlled, which makes it difficult to interpret the specific activity attributed to the blood pressure reduction; and 3) the post-activity monitoring period was limited to only 6-8 waking hours, which may have affected the duration of the blood pressure reduction. Consequently, our next step was to take the field study into the laboratory for a more controlled investigation and to investigate possible mechanisms of the blood pressure reduction.

A sustained reduction in blood pressure following a single bout of aerobic exercise has been defined as post-exercise hypotension [11, 12]. The study of post-exercise hypotension provides evidence not only for the chronic effect of training [13], but for the possible mechanisms of the exercise treatment. The mechanisms of post-exercise hypotension are not fully understood at this time; however, sympathetic modulation has been investigated [11, 12]. Sympathetic modulation describes changes in the balance between sympathetic and parasympathetic influences, or the sympathovagal balance [14]. The autonomic mechanisms of post-exercise hypotension during the activities of daily living have not been investigated.

The purpose of this study was 1) to compare the volume of blood pressure reduction (including the duration and magnitude of the blood pressure reduction) following the accumulation of physical activity to the blood pressure reduction following a single continuous physical activity session; and 2) to observe the association between the reduction in blood pressure and the changes in sympathetic modulation following each physical activity treatment in adults with prehypertension. The following was hypothesized: 1) the reduction in systolic and diastolic blood pressure, measured by the area under the curve for the duration of blood pressure reduction, following the accumulation of physical activity would not be different from the reduction in blood pressure following a single continuous physical activity session in adults with prehypertension; and 2) the magnitude of systolic and diastolic blood pressure reduction would be associated with the change in sympathetic modulation, calculated by the difference in variables of heart rate variability between control and each physical activity treatment in adults with prehypertension; (a) the magnitude of systolic and diastolic blood pressure reduction would be positively correlated with the change in low frequency power of heart rate variability; (b) the magnitude of systolic and diastolic blood pressure reduction would be negatively correlated with the change in high frequency power of heart rate variability; and (c) the magnitude of systolic and diastolic blood pressure reduction would be positively correlated with the change in ratio of low to high frequency power of heart rate variability (that is, an increase in parasympathetic tone and a decrease in sympathetic tone).

## *METHODS*

### Study Design

Fig 1 illustrates the randomized cross-over study design. The two physical activity sessions were separated by at least 7 days to avoid a training effect [15, 16]. The following variables were measured during the 12-hour period following each treatment: 1) blood pressure using ambulatory blood pressure monitoring, 2) heart rate variability using Holter monitoring for sympathetic modulation, and 3) energy expenditure using an accelerometer. The study was approved by the Bloomington Campus Committee for the Protection of Human Subjects at Indiana University. Each participant was given informed consent prior to participation in the study. The study was carried out at the Clinical Exercise Physiology Laboratory in the Department of Kinesiology at Indiana University.

### Subjects

Adults with prehypertension were recruited for this study. Inclusion criteria consisted of a mean screening blood pressure of 120-139 mmHg for systolic blood pressure and/or 80-89 mmHg for diastolic blood pressure. Exclusion criteria included 1) significant cardiovascular disease, 2) significant dysrhythmia; 3) brachial artery bruits, 4) cardiac or renal transplant, or 5) medications such as anti-arrhythmic drugs or low dose muscarinic receptor blockers including atropine and scopolamine that affect the heart rate variability [17]. Clearance by the subjects' primary physician was required prior to participation in the study. The

number of subjects was estimated based on power analysis (power:>0.80; effect size using partial eta squared:>0.41) [18] using the previous study for blood pressure with a similar study design [10] testing a physical activity treatment in adults with prehypertension.

**Blood Pressure Screening**

Three blood pressure measurements were taken in the seated position with a mercury sphygmomanometer on 2 separate days, 3 days apart (a total of six measurements) using an appropriate sized cuff [10, 15, 16]. Each participant was seated for at least 5 minutes in a chair, feet on the floor, and arm supported at heart level [1]. The participant was asked to avoid caffeine, exercise, and smoking for at least 30 minutes prior to measurement [1]. On the first day blood pressure was taken in both arms to detect possible differences due to peripheral vascular disease [10, 15, 16]. The arm with the highest blood pressure was used for the screening [19].

**Maximal Graded Exercise Test**

The purpose of the maximal graded exercise test was to measure physical work capacity to ensure the intensity of the physical activity sessions. A fasting blood draw and a standard resting 12 lead electrocardiogram (EKG) were obtained to establish risk for the graded exercise test. The graded exercise test was performed on a motor driven treadmill at a speed between 2.5 and 4.0 mph. The speed remained constant throughout the test while the grade increased

1.0% every minute until a maximal voluntary effort was achieved. Blood pressure (by auscultation) and heart rate (by EKG) were measured every minute. The EKG was monitored continuously. Expired gases were measured online breath-by-breath using a 2900 Metabolic Measurement Cart (SensorMedics, Corp., Yorba Linda, CA). Peak oxygen uptake ($VO_2$peak) was defined as the highest oxygen uptake ($VO_2$) obtained from the maximal exercise test.

**Treatments**

The treatments included 1) the accumulation of four short sessions of physical activity over a four-hour period, 2) a single continuous physical activity session, and 3) a control. The mode of physical activity was walking on a motorized treadmill and the intensity of physical activity was 50% $VO_2$peak. $VO_2$ was measured during the 2nd through the 4th minutes of each session to confirm the physical activity intensity. If the $VO_2$ were not within $\pm$10% of the target $VO_2$, the work rate was adjusted and $VO_2$ was measured during the 6th through the 8th minutes of the next work interval to confirm the new physical activity intensity. HR (via EKG) and blood pressure (via auscultation) were measured throughout the physical activity treatments. We attempted to end all three treatments at the same time.

Single Continuous Physical Activity Treatment: The single continuous 40-minute physical activity began between 1130 and 1230 hours.

Accumulation of Physical Activity Treatment: The duration of each short session of physical activity was 10 minutes; the first began between 0900 and 0930

hours, the second between 1000 and 1030 hours, the third between 1100 and 1130 hours, and the last between 1200 and 1230 hours.

Control Treatment: For the control treatment the participant reported to the lab between 1200 and 1230 hours, approximately 15 minutes before the time when the monitors would have been activated for the physical activity treatments. Control data were collected for the same 12-hour time period as the other two treatments [10, 15].

**Ambulatory Blood Pressure Monitoring**

The Accutracker II (Suntech Medical Instruments, Inc., Raleigh, NC), validated in accordance to the standards of the British Hypertension Society and the American Association for Medical Instrumentation [20], was used for all ambulatory measurements. The sampling interval was 15 $\pm$ 5 minutes for a 12-hour period following the treatments (1300-0100 hours). One repeat measurement was taken if the first measurement was unsuccessful. The monitor was programmed to take no readings following the 12-hour collection period. The cuff inflation for each measurement was 30 mmHg greater than the previous reading, and the cuff deflation was set at 3 mmHg/second [1].

Ambulatory blood pressure data were manually reviewed for missing and erroneous readings as previously described [10, 15, 16]. Readings were purged if 1) data was missing, 2) systolic blood pressure was lower than diastolic blood pressure, 3) systolic blood pressure was >240 mmHg or <50 mmHg, 4) diastolic blood pressure was >140 mmHg or <40 mmHg, 5) HR was >150 beats/minute or

<40 beats/minute, and/or 6) systolic blood pressure, diastolic blood pressure and heart rate deviated ± 50 and ± 20 mmHg, 30 beats/minute respectively from surrounding values. The numbers of recordings taken and edited were reported.

Ambulatory blood pressure data was averaged each hour for the 12-hour period following each treatment. The duration of blood pressure reduction was determined by calculating the cumulative sum of the blood pressure reduction for each hour as previously reported [10]. The cumulative sum of blood pressure reduction was then plotted for each hour with the 95% confidence limits for the slope. The duration of the blood pressure reduction was considered to be the time period in which the blood pressure reduction remained within the 95% confidence limits of the regression. Once the duration was determined, the magnitude of the blood pressure reduction was averaged over the duration of the reduction found for each activity treatment and was compared to the respective periods from the control treatment [10].

The areas of the blood pressure reduction were used to compare the efficacy of the accumulation vs. the continuous physical activity treatments. The area of the blood pressure reduction was defined as the area between the physical activity and control blood pressure curves for the duration of blood pressure reduction [10, 15]. The area between the blood pressure curve and the time axis (x-axis) was calculated by summing the area of successive trapezoids, corresponding to each blood pressure reading. The total area below the physical activity treatment curve was subtracted from the total area under the control curve to obtain the area between the curves.

**Holter Monitoring**

The Aria Digital Recorder (Del Mar Reynolds Medical, Inc., Irvine, CA) was used to observe sympathetic modulation through heart rate variability. The EKG data were collected for the 12-hour period following each treatment. The data from the Aria Digital Recorder were scanned on a computer-assisted Holter system (Impresario, Solo Holter analysis software, Del Mar Reynolds Medical, Inc., Irvine, CA) for variables of heart rate variability. Manual editing of the R-R interval data was performed to ensure correct identification and classification of every QRS complex [17]. Artifact and ectopic beats were removed for the R-R interval calculation. The data were then used for the power spectral analysis of heart rate variability.

Frequency-domain measures of heart rate variability were assessed using the fast Fourier transform. The total power was calculated by the standard deviation of the R-R interval (<0.1 Hz). Heart rate variability of the total nominal 12-hour record was computed using the whole range of high frequency power (0.15-0.40 Hz), low frequency power (0.04-0.15 Hz), and very low frequency (0.003-0.04 Hz) power. Normalized values (expressed as %) were calculated for low frequency power and high frequency power. Normalized units represent the relative value of each power component in proportion to the total power minus the very low frequency component. The ratio of low frequency to high frequency was also determined. The changes in values of heart rate variability were calculated as (values of the control treatment – values of each physical activity treatment). To determine the association with the blood pressure reduction,

these variables of heart rate variability were averaged for the duration of blood pressure reduction.

**Accelerometer**

Energy expenditure was measured to statistically control for variations in activities of daily living as a covariate if significant difference was found among the 12 hours of monitoring following the three treatments. An RT3 (Stayhealthy, Inc., Monrovia, CA), three-dimensional (tri-axial) accelerometer, was used for a 12-hour collection period following all three treatments. The Output from each accelerometer was reported along with a composite three-dimensional signal called vector magnitude. The software provides an estimation of activity and total energy expenditure based on age, height, weight, and gender of the individual. The RT3 was programmed (using mode 3) to sample data every second and to average data over a one-minute period. Energy expenditure was averaged for the 12-hour period.

**Preparation of Subjects**

The ambulatory blood pressure cuff was worn on the non-dominant arm. Seven EKG electrodes (three for ambulatory blood pressure monitor and four for Holter monitor) were placed on the chest. The RT3 was firmly attached to a belt on the hip at the anterior axillary line of the dominant leg. Participants were asked to document the following: 1) time of sleep, 2) time at work, 3) time of meals, and 4) time and type of leisure physical activity. They were also asked to

do the similar routines for the activities of daily living following all treatments. Instructions included 1) not to exercise, 2) not to take a shower, 3) not to use an electric blanket, 4) not to operate a lawn mower, a vacuum cleaner or any equipment which causes vibration, 5) to replace electrodes with new electrodes when electrodes became loose, and 6) to relax and straighten out the arm during the recording interval for the entire 12-hour period.

**Statistical Analysis**

Data was expressed as means $\pm$ standard error of the mean (SE). Statistical analyses were performed using descriptive statistics, paired t-tests, and analysis of variance (ANOVA) for repeated measures. Descriptive statistics were performed on the variables of sex, age, body mass index (BMI), screening systolic blood pressure and diastolic blood pressure, and $VO_2$peak. A one-way ANOVA with repeated measures was used to test the differences in energy expenditure from the accelerometry for the activities of daily living following each treatment. Paired t-tests were used to test the difference in the magnitude of the blood pressure reduction (mean blood pressure for the respective duration) between each physical activity and the control treatment, and to compare the area of the blood pressure reduction between the two activity treatments.

Pearson correlations were used to evaluate the contribution of confounding variables (such as amount of physical activity, age and BMI) on magnitude of the blood pressure reduction. Pearson correlations were also used to investigate the association between the magnitude of blood pressure reduction

and the change in sympathetic modulation. The level of significance was $P<0.05$. The SPSS software (SPSS 13.0) was used for all statistical analyses.

## *RESULTS*

### Subjects

Twenty-six adults were screened for the study; five were found to be ineligible during the blood pressure screening process (four presented with normal blood pressure and one presented with hypertension). Twenty-one adults with prehypertension who were qualified based on the screening process. One participant did not complete the study because of time constraints. Twenty adults with prehypertension completed the study. Demographics of the participants are summarized in Table 1.

### Physical Activity Stimulus

The 20 participants who completed the study performed a maximal voluntary effort on the exercise test as verified by reaching 107.7 ± 1.3% predicted maximal heart rate. Each physical activity treatment was separated by 16.7 ± 2.3% days. The intensities of both activity treatments were similar (accumulation = 51.9 ± 0.6% of $VO_2$peak; continuous = 51.7 ± 0.6% of $VO_2$peak).

### Energy Expenditure following all Three Treatments

The energy expenditure was measured to determine the consistency of the activities of daily living during the 12-hour monitoring period following each

treatment session. No significant difference (P=0.894) was found among the three treatment sessions: the energy expenditures for 12 hours following the control, the accumulation of physical activity, and the single continuous physical activity treatment sessions were 351.1 ± 38.3 kcal, 348.5 ± 32.6 kcal, and 335.1 ± 36.3 kcal, respectively. Therefore, blood pressure data were not examined using energy expenditure as a covariate.

**Blood Pressure Reduction**

Ambulatory blood pressure monitoring data are summarized in Table 2. There was no significant difference in the number of blood pressure measurements and the percent of blood pressure measurements analyzed among the three ambulatory sessions. The cumulative sums of the hourly mean systolic blood pressure and diastolic blood pressure reduction for the accumulation of physical activity and the single continuous physical activity were plotted to determine the duration of the blood pressure reduction in Fig 2. The durations of the systolic and diastolic blood pressure reductions were both 7 hours following the single continuous physical activity. The durations of the systolic and diastolic blood pressure reductions following the accumulation of physical activity, however, were 11 hours and 10 hours respectively.

The hourly mean systolic and diastolic blood pressures following all three treatments as well as the area between the treatment and control blood pressure curves are illustrated in Fig 3. Both the 7-hour mean systolic blood pressure (-5.6 ± 1.6 mmHg; P=0.002) and 7-hour mean diastolic blood pressure (-3.1 ± 0.2

mmHg; P=0.020) following the single continuous physical activity session were significantly decreased from the blood pressure following the control treatment for the corresponding time periods. Similarly, the 11-hour mean systolic blood pressure (-5.4 ± 1.7 mmHg; P=0.005) and 10-hour mean diastolic blood pressure (-3.4 ± 1.3 mmHg; P=0.022) following the accumulation of physical activity were also decreased from the blood pressures following the control treatment for the corresponding time periods. In addition, the area of the systolic blood pressure reduction following the accumulation of physical activity treatment was significantly greater (P=0.045) than the area of the systolic blood pressure reduction following the single continuous physical activity treatment. No significant difference was found in the area of diastolic blood pressure reduction between the two activity treatments.

**Association between the Magnitude of Blood Pressure Reduction and the Change in Sympathetic Modulation**

The association between the magnitude of blood pressure reduction and the change in sympathetic modulation as measured by heart rate variability is illustrated in Fig 4 and Fig 5. For the continuous physical activity (Fig 4), the difference in low/high frequency ratio was only significantly correlated with the magnitude of diastolic blood pressure. For the accumulation of physical activity (Fig 5), however, the differences in normalized low frequency and high frequency between the control and the physical activity treatments were significantly correlated with the magnitude of the systolic blood pressure while the differences

in normalized low frequency, high frequency, and low/high frequency ratio were significantly correlated with the magnitude of the diastolic blood pressure.

## *DISCUSSION*

The purpose of this study was 1) to compare the magnitude and duration of blood pressure reduction following the accumulation of physical activity to the blood pressure reduction following a single continuous physical activity session; and 2) to observe the association between the reduction in blood pressure and the changes in sympathetic modulation following two physical activity treatments in adults with prehypertension. This is the second study to investigate the blood pressure reduction as a primary outcome following the accumulation of physical activity in prehypertension [10]. Strengths of our study include the target population and the study design and methods. In our study unexpected, yet provocative findings were obtained. The main findings were 1) a greater reduction in systolic blood pressure following the accumulation of physical activity than following a single continuous physical activity session in adults with prehypertension, and 2) the association between the reduction in systolic and diastolic blood pressure and the changes in sympathetic modulation (a decrease in sympathetic tone and an increase in parasympathetic tone) independent of confounding variables such as physical activity, age, and BMI.

Prehypertension has been identified as a critical population, who requires intervention to treat as well as to prevent progression to hypertension [1]. Although lifestyle modification, including the accumulation of physical activity, is

the only recommended treatment for prehypertension at this time [1], supporting literature is limited [10]. Only one study [10] exists focusing on the efficacy of the accumulation of physical activity as a treatment for prehypertension. Thus, our study of adults with prehypertension is warranted.

Our study design and methods are distinctive in 1) the acute treatment model, 2) the target population, 3) the accumulation of several short physical activity sessions, and 4) building on our previous field study. First, the acute rather than chronic training treatment model was chosen for this study. Acute studies can be justified solely on the fact that no long-term or training study exists focusing on prehypertension. In addition, the acute effects of exercise in blood pressure reduction are considered to contribute to the chronic or training effects in hypertension [13]. The utilization of an acute paradigm also allows for a more efficacious study with possible variations in the physical activity stimulus.

In prehypertension, the accumulation of physical activity has been recommended [1] as a treatment despite limited evidence of its effectiveness [10]. In a recent meta-analysis of exercise training on blood pressure [5], 33 studies were identified as focusing on prehypertensive groups. Further inspection of these studies revealed, however, that the targeted population was not limited to prehypertensive subjects even though their average blood pressure was in the range of prehypertension. All of these groups were comprised of mixed prehypertension with normotension or prehypertension with hypertension. Thus, the results of this meta-analysis [5] can be challenged because the target

population was not within the definition of prehypertension. It is important to investigate the efficacy of physical activity specific to adults with prehypertension.

Supporting evidence is also limited on the efficacy of the accumulation of physical activity in the treatment of prehypertension and hypertension. Two training studies [21, 22] attempted, but did not document or control for the accumulation of the activity. Our current study not only focused on a comparison of the accumulation of physical activity vs. continuous sessions, but controlled the mode, intensity, and duration of physical activity well.

In the analysis of the data, the determination of the duration of the blood pressure reduction and the utilization of the area of the blood pressure reduction are among the strengths developed from our previous study [10, 15]. Utilizing the 95% confidence limits for the accumulative sum of the reduction allows for an objective determination of duration. In addition, the area under the curve, which represents the total volume (magnitude x duration) of the blood pressure reduction, was used to standardize the two treatments for comparison of the blood pressure reduction. Both of these variables were used to compare the blood pressure reduction between the two physical activity treatments yielding more precise results.

The restraints of our previous field study [10] on lifestyle physical activity in prehypertension and hypertension were controlled in the present laboratory design. First, we utilized a 40-minute physical activity treatment instead of 4-6 hours. Second, we presented a single, common and popular mode [23] of physical activity, walking. Third, the monitoring period following the physical

activity treatments was extended from 6 hours to12 hours to provide a longer time to monitor the duration of blood pressure reduction before sleep. Average nighttime blood pressures for hypertensive adults who exhibit nocturnal dipping are within normal pressures and do not exhibit a reduction following exercise [15]. We have found that adults with prehypertension exhibit the similar nocturnal dipping pattern. Because the duration of any blood pressure reduction would be limited by the nighttime hours, we extended the monitoring time from 6 hours to12 hours. An additional advantage to extending the monitoring period was to control for the diurnal variation of the blood pressure. Blood pressure is highest in the afternoon/evening hours and lowest in the nighttime [24]. By focusing our monitoring time to a period known to exhibit high pressures, a reduction in blood pressure would be more easily detected because a reduction in blood pressure is related to elevation of the initial pressures [7]. This design optimized the diurnal nature of the blood pressure as well as the timing of the blood pressure reduction. In the real world, the physical activity would be accumulated throughout the day rather than the four hour period studied in this investigation and still may have reduce blood pressure when applied in a chronic application [25].

The blood pressure reduction found in the present study was unexpected. We expected the blood pressure reduction to be similar for both activity treatments, based on previous literature in fractionization [25-28]. Fractionization [29] is the term used to describe the comparison between a single continuous exercise/ physical activity session to several short bouts of the exercise/ physical

activity. Fractionization has been utilized to observe variables of health and fitness, such as maximal oxygen uptake ($VO_2$max) [25, 26] and blood lipids [27, 28]. Several short bouts of exercise were reported to be as effective as one continuous exercise in these variables [25-28]. Although blood pressure is one of major risk factors of the coronary heart disease, it has not been the focus of the fractionization literature as a primary outcome.

Blood pressure has been observed as a secondary outcome in fractionized exercise training studies where 2-3 short sessions were compared to one continuous exercise [25, 26]. Murphy and Hardman [25] randomly assigned 12 women to 1) 3 x 10-minute walks, 2) 1 x 30-minute walk at 70-80 % of maximal heart rate or 3) control group for 10 weeks. Although the blood pressure reduction found in this study was not statistically significant, it exhibited similar trends to ours; the 3 x 10-minute group reduced systolic blood pressure by 7.4 ± 7.3 mmHg whereas the 1 x 30-minute group reduced systolic blood pressure by 4.6 ± 5.9 mmHg. Murphy and Hardman [25] did not find a significant blood pressure reduction, which may be attributed to their lack of statistical power. Asikainen et al. [26] also investigated blood pressure reduction after 15-weeks of training; two short bouts vs. one continuous walking (65% of $VO_2$max). Similarly, no significant blood pressure reduction was found in each exercise group compared to the control group, but diastolic blood pressure was reduced (3.0 mmHg) when the exercise groups were combined. On the other hand, subjects in both of these training studies included normotensive and hypertensive subjects, exhibiting a wide range of blood pressures. The inclusion of non-

responding normotensive subjects may have confounded the results. Not only was blood pressure a primary outcome in our study, adults with prehypertension were the target population, thus optimizing our findings.

Chronic exercise is well known for its ability to restore impaired autonomic nervous system function in various populations [17, 30], including hypertension [31]. The mechanisms of blood pressure reduction following acute exercise are not fully understood at this time, however, sympathetic modulation has recently received more focus as one of the possible mechanisms [11, 12]. Sympathetic modulation has been examined only for a relatively short (15-180 minutes) period of time [32] following acute exercise. Recently, the change in sympathetic modulation was observed several hours after cessation of acute submaximal exercise [33]. In addition, the blood pressure reduction following acute exercise persists up to 11-12 hours in hypertension [2]. Thus, we observed 7-hour to12-hour heart rate variability and found significant association between the reduction in blood pressure and the change in sympathetic modulation. The involvement of the autonomic nervous system as a possible mechanism for the blood pressure reduction following a single bout of exercise has been found in other studies [34-36].

The accumulation of physical activity led to a greater systolic blood pressure reduction than a single continuous physical activity in prehypertension. Results of our study indicate as little as four 10-minute walking sessions per day is effective in reducing systolic and diastolic blood pressure in prehypertension. A 5 mmHg reduction in systolic blood pressure has been reported to substantially

reduce mortality; 14% reduction in stroke, and 9% reduction in coronary heart disease [1]. An immediate and favorable response associated with one day of physical activity may encourage the public to participate in physical activities in one's daily routine. Several 10-minute walking sessions might fit more easily into one's daily routine than a single long continuous session. For the future studies, chronic training effects of the accumulation of physical activity as well as adherence to physical activity need to be investigated in prehypertension.

***ACKNOWLEDGEMENTS***

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***FIGURE 1.*** Design including dependent variables and participants flow of the study.

Fig. 1

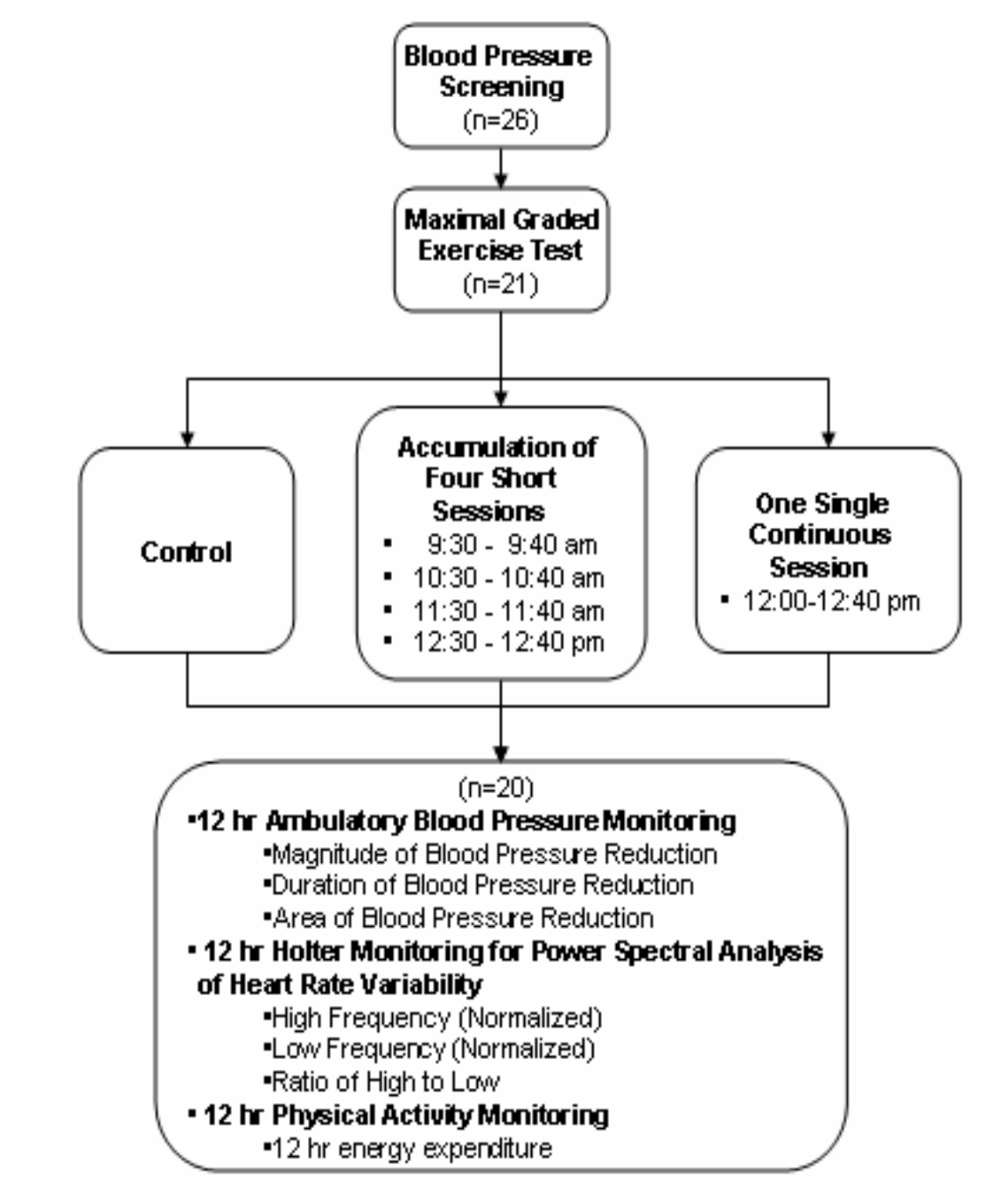

Blood Pressure Screening
(n=26)
Maximal Graded Exercise Test
(n=21)
Control
Accumulation of Four Short Sessions
9:30 - 9:40 am
10:30 - 10:40 am
11:30 - 11:40 am
12:30 - 12:40 pm
One Single Continuous Session
12:00-12:40 pm
(n=20)
12 hr Ambulatory Blood Pressure Monitoring
Magnitude of Blood Pressure Reduction
Duration of Blood Pressure Reduction
Area of Blood Pressure Reduction
12 hr Holter Monitoring for Power Spectral Analysis of Heart Rate Variability
High Frequency (Normalized)
Low Frequency (Normalized)
Ratio of High to Low
12 hr Physical Activity Monitoring
12 hr energy expenditure

***TABLE 1. DEMOGRAPHICS OF SUBJECTS***

| **Variables** | |
|---|---|
| N | 20 |
| Sex (men/women) | 15/5 |
| Race | 18 Caucasian<br>2 Asian |
| Age (years) | 47.2 ± 2.9 |
| Weight (kg) | 84.5 ± 4.4 |
| Height (cm) | 176.3 ± 1.7 |
| Body mass index (kg/m2) | 27.0 ± 1.2 |
| $VO_2$peak (ml/kg/min) | 34.5 ± 1.6 |
| Screening systolic blood pressure (mmHg) | 131.9 ± 1.1 |
| Screening diastolic blood pressure (mmHg) | 82.5 ± 1.4 |

Values were expressed as mean ± S.E.

***TABLE 2. AMBULATORY BLOOD PRESSURE MONITORING***

| | ***Control Treatment*** | ***Accumulation of Physical Activity*** | ***Single Continuous Physical Activity*** |
|---|---|---|---|
| **Starting Time** | 12:42 ± 0:05 | 12:48 ± 0:05 | 12:56 ± 0:04 |
| **Number of Blood Pressures Taken** | 55.2 ± 1.3 | 52.4 ± 1.2 | 53.4 ± 1.1 |
| **Percent of Blood Pressures Analyzed** | 93.8 ± 1.6 | 92.0 ± 2.3 | 91.6 ± 1.8 |

Values were expressed as mean ± S.E.

***FIGURE 2.*** Regression (solid line) and 95% confidence limits (dotted line) for the slope of the initial blood pressure (blood pressure) reduction following a single continuous physical activity (upper graph) and the accumulation of physical activity (lower graph) and in adults with prehypertension. See text for the calculation used to determine the plot. The duration of blood pressure reduction (↑) was determined to be the time where the accumulated hourly blood pressure reduction remained within the 95% confidence limit.

Fig. 2

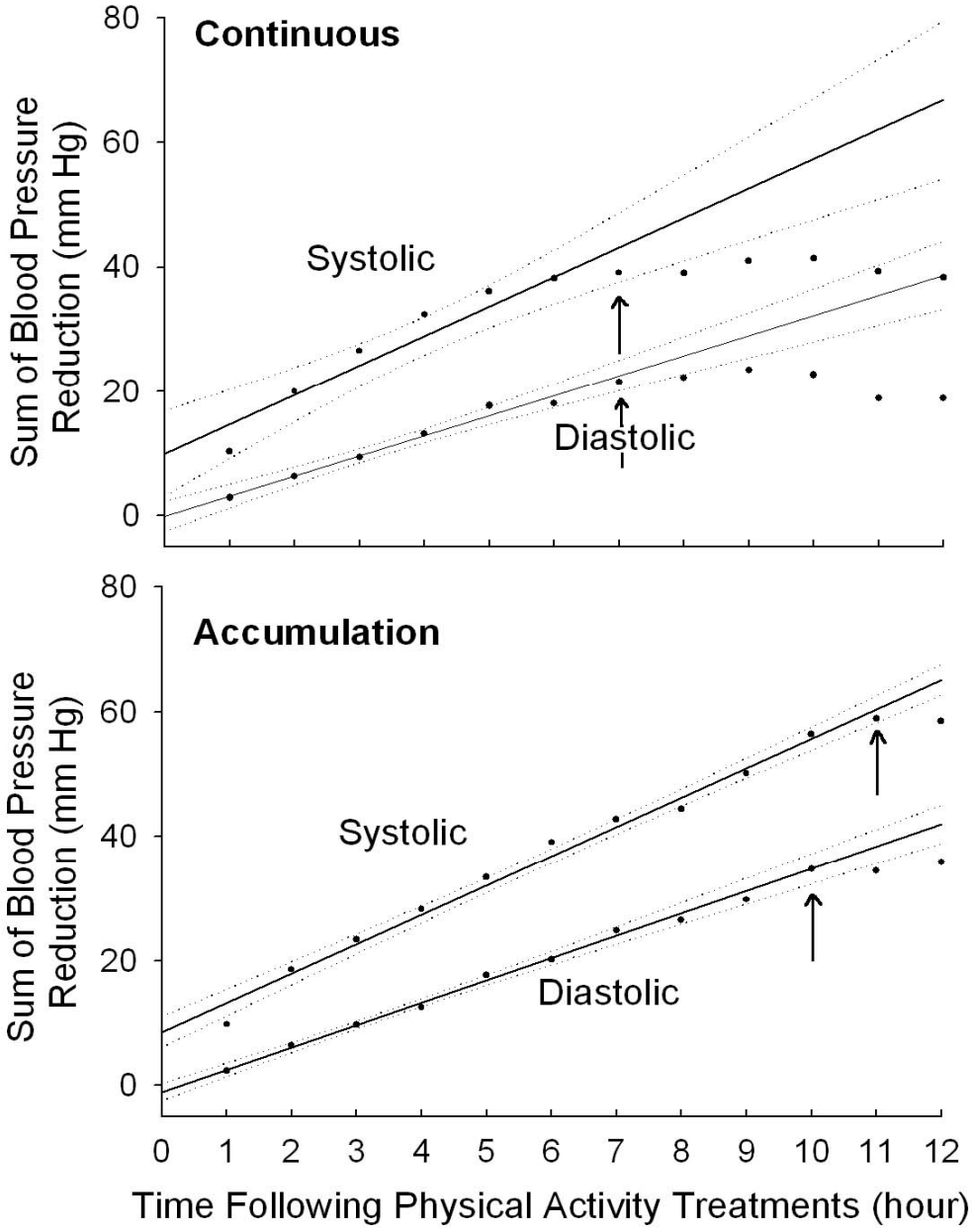
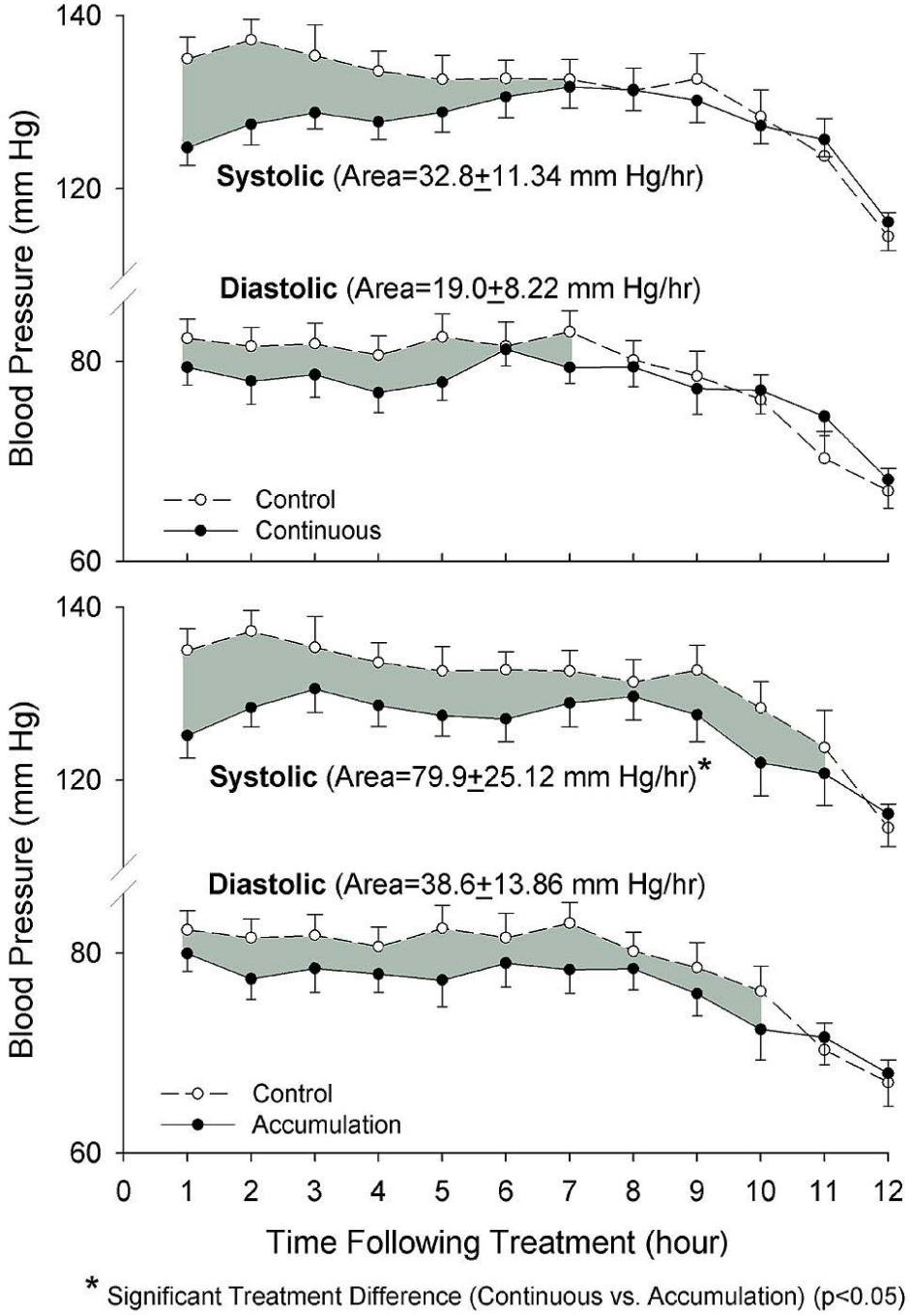

Continuous
Systolic
Diastolic
Sum of Blood Pressure Reduction (mm Hg)
80
60
40
20
0
Accumulation
Systolic
Diastolic
Sum of Blood Pressure Reduction (mm Hg)
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12
Time Following Physical Activity Treatments (hour)

***FIGURE 3***. Hourly systolic and diastolic blood pressure following the single continuous physical activity session (●) and control treatment (○) (upper graph) and following the accumulation of physical activity (●) and control treatment (○) (lower graph) in adults with prehypertension.

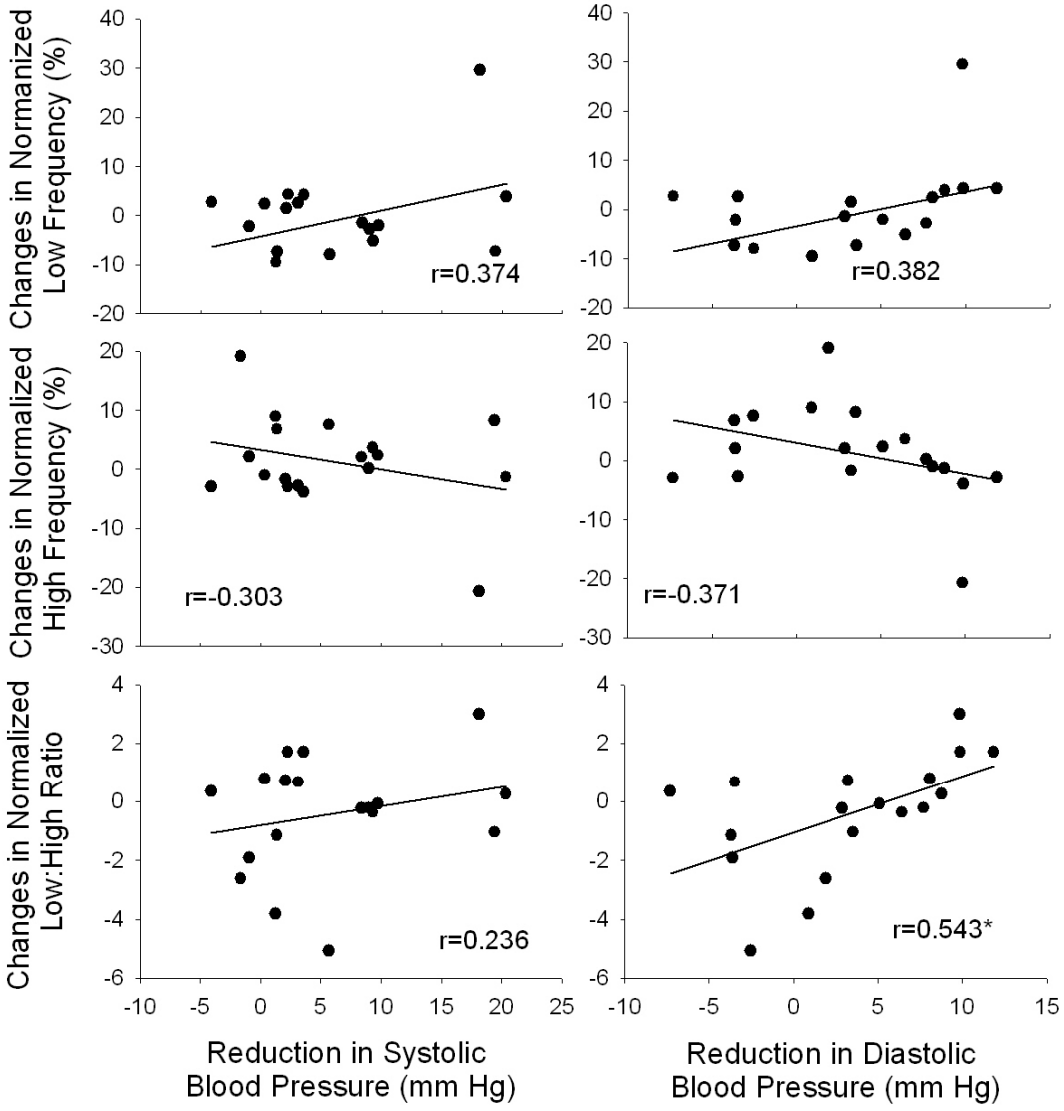
Fig. 3




* Significant Treatment Difference (Continuous vs. Accumulation) ($p<0.05$)

***FIGURE 4.*** The association between the reduction in blood pressure and the changes in sympathetic modulation following a single continuous physical activity session. The changes in sympathetic modulation were calculated as (values of heart rate variability from the control treatment – values of heart rate variability from a single continuous physical activity session).

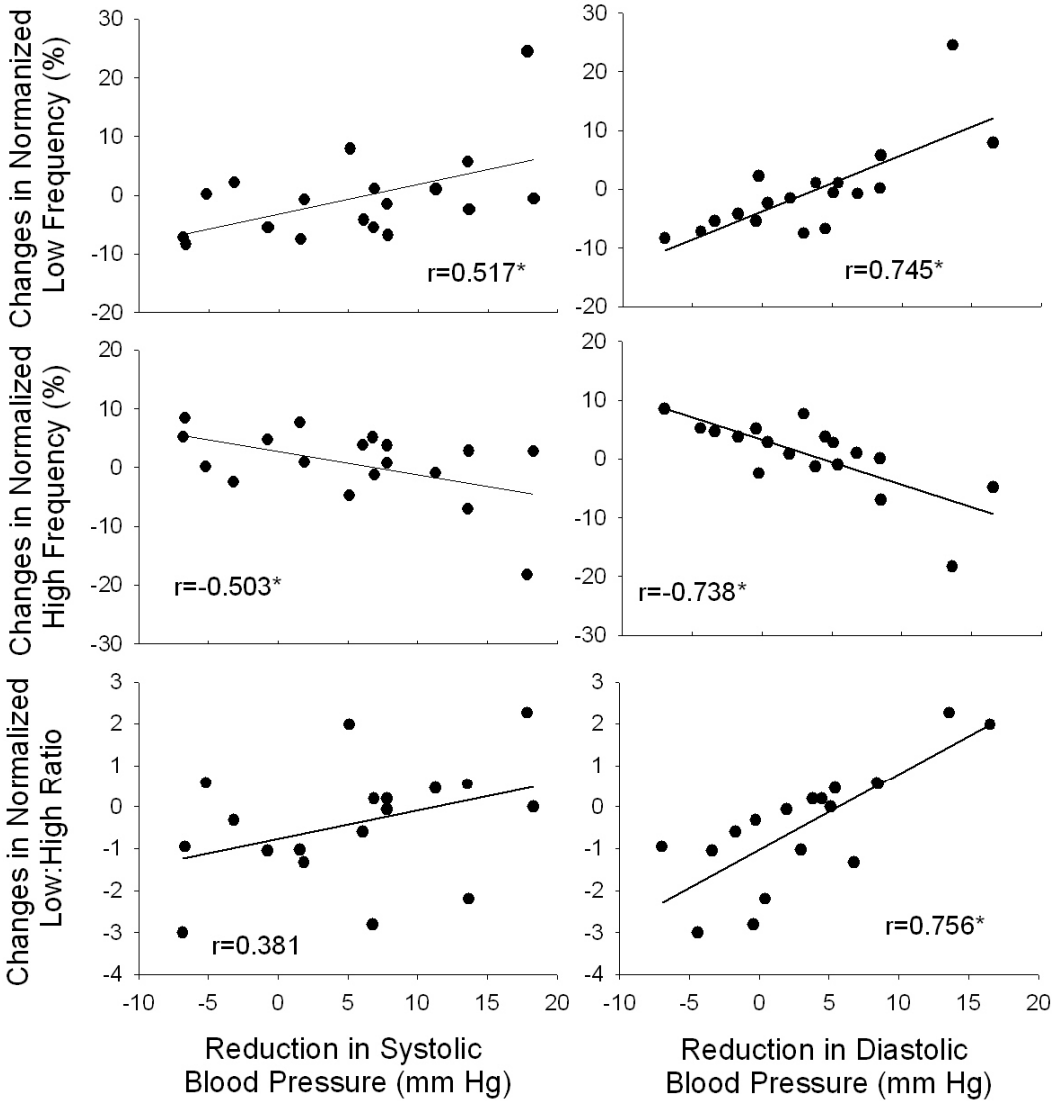
Fig. 4




* Significant Correlation ($p<0.05$)

***FIGURE 5.***. The association between the reduction in blood pressure and the changes in sympathetic modulation following the accumulation of physical activity. The changes in sympathetic modulation were calculated as (values of heart rate variability from the control treatment – values of heart rate variability from a single continuous physical activity session).

Fig 5.




* Significant Correlation ($p<0.05$)

# MANUSCRIPT

***Accumulation of Physical Activity: Blood Pressure Reduction between Sessions***

**Running Title**: Accumulation of physical activity

***ABSTRACT***

The accumulation of physical activity, recommended as a treatment for both prehypertension and hypertension, has been found to effectively reduce blood pressure (BP) in prehypertension and hypertension. Yet, the BP response among several short sessions within the accumulation of physical activity has not been examined in the treatment for prehypertension and hypertension. **Purpose:** The purpose of the study was 1) to investigate the BP reduction during the rest periods following each successive short session within the accumulation of physical activity over a three-hour period in prehypertensive adults; and 2) to observe the role of sympathetic modulation during the rest periods following each short session. **Methods:** Prehypertensive adults (131.9±1.05/83.0±1.63 mm Hg) participated in the study. BP, using ambulatory monitoring, and sympathetic modulation via heart rate variability (HRV; Holter monitoring) were measured during a baseline and the rest periods following three short physical activity sessions (3 x 10-minute treadmill walks at 50% of $VO_2$peak; at least 50-minute apart). Sympathetic modulation was reported as normalized low-frequency, high-frequency power and the ratio of low to high frequency power of HRV. Variables of BP and HRV were averaged for the baseline period and for the rest periods following each short session. One-way ANOVA with repeated measures was used to test the differences over time in the BP and HRV ($p<0.05$). Tukey test was used for post-hoc comparison. **Results:** A significant main effect was found in systolic BP ($p=0.039$) while none was found in diastolic BP ($p=0.666$). Systolic BP was significantly decreased following the third short session. No significance

was found in any of the sympathetic modulation variables. **Conclusion:** Successive walking sessions presented additive effects on systolic BP reduction while they did not affect either diastolic BP or sympathetic modulation in prehypertension.

**Key Words:** Ambulatory Blood Pressure, Postexercise Hypotension, Fractionization of Exercise, Heart Rate Variability, Prehypertension

**Paragraph Number 1** Hypertension, the most common primary diagnosis in the U.S. (4), is associated with an increased incidence of all-cause and cardiovascular mortality (5, 29). In 2003, 45 million adults with prehypertension were added to the patient population in need of treatment for high blood pressure (5). Lifestyle modification (2, 5), including regular physical activity, is the only recommended treatment for prehypertension. It is also the only recommended treatment for the prevention of prehypertension progressing to hypertension (27). The physical activity recommendation for the treatment of both prehypertension and hypertension includes the accumulation of 30 minutes or more of moderately intense physical activity on most, preferably all, days of the week (2, 5). Yet, the scientific evidence has neglected the accumulation aspects of physical activity in the treatment of hypertension (2, 5, 29). The American College of Sports Medicine Position Stand on exercise and hypertension (2) has stated that there is limited evidence regarding the accumulation of several short sessions of physical activity on blood pressure reduction. It is this limited scientific evidence that has led to our work in the accumulation of physical activity as a treatment for prehypertension (17, 19).

**Paragraph Number 2** We have investigated the effects of the accumulation of physical activity in prehypertension (17, 19) and hypertension (17). First, we (17) examined the effects of the accumulation of lifestyle physical activity in prehypertension and hypertension. The accumulation of lifestyle physical activity over a 12-hour period significantly reduced systolic blood pressure in adults with

prehypertension (-6.6 ± 2.3 mm Hg for 6 hours) and hypertension (-12.9 ± 4.3 mm Hg for 8 hours). For the second study (19), we took this field study (17) into the laboratory for a more controlled investigation. We compared the blood pressure reduction following the accumulation of physical activity (four 10-minute walks at 50% of peak oxygen uptake ($VO_2$peak)) to the blood pressure reduction following a single continuous physical activity session (one 40-minute walk at 50% of $VO_2$peak) in prehypertension. We also examined the sympathetic modulation as a possible mechanism for blood pressure reduction following the accumulation of physical activity. Our findings were provocative. Greater reductions in both systolic and diastolic blood pressures were found following the accumulation of physical activity (-5.4 ± 1.7 mm Hg of systolic for 11 hours; -3.4 ± 1.3 mm Hg of diastolic for 10 hours) than following a single continuous physical activity session (-5.6 ± 1.6 mm Hg of systolic for 7 hours; -3.1 ± 0.2 mm Hg of diastolic for 7 hours) in adults with prehypertension. From our two previous studies (17, 19), the accumulation of physical activity on blood pressure reduction was found to be effective. Yet, the blood pressure response between the short sessions during the accumulation of physical activity has not been examined.

**Paragraph Number 3** The investigation of the rest periods between the short sessions during the accumulation of physical activity/exercise has had limited scrutiny. The accumulation of physical activity has been compared to the continuous activity in fractionated exercise designs to observe variables of fitness

and health outcomes such as maximal oxygen uptake ($VO_2$max) (3, 15), excess post-exercise oxygen consumption (EPOC) (1, 10), blood lipids (7, 15, 16), and blood pressure (16, 19). Despite many studies utilizing fractionated exercise, the rest periods between the activity sessions were observed only in a few studies focusing on EPOC (1, 10). In these EPOC studies, each short session was compared and found to yield similar responses (1, 10). In our previous studies, the blood pressure was effectively decreased following the accumulation of physical activity (17, 19); yet, the blood pressure patterns for the rest periods between the short sessions during the accumulation of physical activity has not been observed.

**Paragraph Number 4** In one of our previous studies (19) on the accumulation of physical activity, sympathetic modulation was associated with the reduction in blood pressure. A sustained reduction in blood pressure following a single bout of aerobic exercise has been defined as post-exercise hypotension (11). The mechanisms of post-exercise hypotension are still not fully understood. Sympathetic modulation has recently received more focus as one of the possible mechanisms of post-exercise hypotension (9, 14). Sympathetic modulation describes changes in the balance between sympathetic and parasympathetic influences, or the sympathovagal balance (8, 21). Although sympathetic modulation has been reported to be associated with post-exercise hypotension during the activities of daily living following the accumulation of physical activity

(19), sympathetic modulation has not been examined between the short sessions.

**Paragraph Number 5** The purpose of the study was 1) to investigate the blood pressure reduction during the rest periods following each successive short session within the accumulation of physical activity over a 3-hour period in adults with prehypertension, and 2) to study sympathetic modulation during the rest periods following each short physical activity session over a 3-hour period in adults with prehypertension. We hypothesized 1) the systolic and diastolic blood pressures following each successive short physical activity session would be lower than the blood pressure of previous sessions in adults with prehypertension, and 2) the sympathetic modulation, measured by power spectral analysis of the heart rate variability, would be different following each successive short physical activity session in adults with prehypertension; (a) the normalized low frequency power of heart rate variability would be lower following each successive short physical activity session, (b) the normalized high frequency power of heart rate variability would be higher following each successive short physical activity session, (c) the low to high frequency power of heart rate variability would be lower following each successive short physical activity session.

## *METHODS*

**Paragraph Number 6** The study design is shown in Figure 1. Adults with prehypertension participated in the study. Ambulatory blood pressure and Holter monitoring began for a baseline period prior to the physical activity sessions, continued during physical activity and rest periods, and continued for 12 hours following the end of the last physical activity session. For physical activity, subjects were asked to walk on a motor-driven treadmill for 10 minutes at 50% of peak oxygen uptake ($VO_2$peak) four times in a 4-hour period. Subjects were seated for the rest period between the first three activity sessions. After the fourth session, instead of a seated rest period, subjects left the laboratory and engaged in their activities of daily living for 12 more hours. The blood pressure reduction and sympathetic modulation following the end of physical activity stimulus were reported for a 12-hour period in other study (19). In the present study we evaluated blood pressure reduction and sympathetic modulation during the rest periods following three successive short sessions. The study was approved by the Bloomington Campus Committee for the Protection of Human Subjects at Indiana University. Written informed consent was obtained from each subject prior to participation in the study. The study was carried out at the Clinical Exercise Physiology Laboratory in the Department of Kinesiology at Indiana University.

## Subjects

**Paragraph Number 7** Adults with prehypertension were recruited for this study. Inclusion criteria consisted of 120-139 mm Hg of a mean systolic screening blood pressure and/or 80-89 mm Hg of a mean diastolic blood pressure taken from at least two readings on two separate days, three days apart. Exclusion criteria included 1) significant cardiovascular disease, 2) significant dysrhythmia (24, 25), 3) brachial artery bruits (24, 25), 4) cardiac or renal transplant (24, 25), or 5) medications such as anti-arrhythmic drugs or low dose muscarinic receptor blockers including atropine and scopolamine that affect the heart rate variability (22). Clearance by the participants' primary physician was required prior to participation in the study.

**Paragraph Number 8** The number of subjects was estimated based on power analysis (power:>0.80; effect size using partial eta squared:>0.41) (12) using the previous study for blood pressure with a similar study design (17) testing a physical activity treatment in adults with prehypertension.

## Blood Pressure Screening

**Paragraph Number 9** For all participants three blood pressure measurements were taken in the seated position on two separate days, three days apart (a total of six measurements) using a mercury sphygmomanometer (17). Each participant was seated for at least five minutes in a chair, feet on the floor, and

arm supported at heart level (5). The participant was asked to avoid caffeine, exercise and smoking for at least 30 minutes prior to measurement (5). An appropriate sized cuff (cuff bladder encircling at least 80% of the arm) was used to ensure accuracy (5). On the first day blood pressure was taken in both arms to detect possible differences due to peripheral vascular disease (28). The arm with highest blood pressure was used for the screening (28).

### Maximal Graded Exercise Test

**Paragraph Number 10** The purpose of maximal graded exercise test was to measure physical work capacity to ensure the intensity of the physical activity sessions. A fasting blood draw and a standard resting 12 lead electrocardiogram (EKG) preceded the maximal graded exercise test to establish risk for the graded exercise test. The graded exercise test was performed on a treadmill with a speed between 2.5 and 4.0 mph. The speed remained constant throughout the test while the grade increased 1.0% every minute until a maximal voluntary effort was achieved. Blood pressure (by auscultation) and heart rate (by EKG) was measured every minute. The EKG was monitored continuously. Expired gases were measured on-line breath-by-breath using a 2900 Metabolic Measurement Cart (SensorMedics, Corp., Yorba Linda, CA). $VO_2$peak was obtained during the symptom-limited maximal exercise test. $VO_2$peak is defined as the highest $VO_2$ obtained from the symptom-limited maximal exercise test.

## Treatments

**Paragraph Number 11** A 15-minute baseline period preceded the treatment. The focus of the treatment for this study was the three rest periods following the first three short sessions of physical activity over a three-hour period. The mode of physical activity was walking on a motorized treadmill and the intensity of each physical activity session was at 50% $VO_2$peak. Oxygen uptake ($VO_2$) was measured during the 2$^{nd}$ through the 4$^{th}$ minutes of each walk to confirm the intensity of physical activity. The work rate was adjusted if it was not within $\pm$10% of the target $VO_2$. Then, $VO_2$ was measured during the 6$^{th}$ through the 8$^{th}$ minutes of the next work interval to confirm the new physical activity intensity. Heart rate (via EKG) and blood pressure (via auscultation) was measured throughout the physical activity treatment.

**Paragraph Number 12** Baseline Period: The participant reported to the lab between 0830 and 0900 hours approximately 15 minutes before the time when the monitors would be activated for the study. After the participant wore the monitors, the participant was in the seated position for a 15-minute baseline period.

**Paragraph Number 13** Accumulation of Short Physical Activity Treatment: The duration of each short physical activity session was 10-minute; the first between 0900 and 0930 hours, the second between 1000 and 1030 hours, and the third

between 1100 and 1130 hours. Each short session was followed by the 50-minute rest period in the seated position.

### Ambulatory Blood Pressure Monitoring

**Paragraph Number 14** The Accutracker II (SunTech Medical Instruments, Inc., Raleigh, NC) was used for the ambulatory blood pressure measurements. The Accutracker II has been validated in accordance to the standards of the British Hypertension Society and the American Association for Medical Instrumentation (23). The ambulatory blood pressure cuff was worn on the non-dominant arm. Electrode wires and blood pressure tubing were taped securely to the chest. The cuff inflation for each measurement was 30 mm Hg greater than the previous reading, and the cuff deflation was set at 3 mm Hg·second$^{-1}$ (5). The sampling intervals were 1) every 5 minutes for the 15-minute baseline period; 2) every 5 minutes for the first 20 minutes of the 50-minute rest period among three short sessions of physical activity; and 3) every 10 minutes for the remainder of the 50-minute rest period among three short sessions of physical activity. No repeat measurements were taken.

**Paragraph Number 15** Ambulatory blood pressure data was manually reviewed for missing and erroneous readings (17). Readings were purged if 1) data was missing; 2) systolic blood pressure was lower than diastolic blood pressure; 3) systolic blood pressure was >240 mm Hg or <50 mm Hg; 4) diastolic blood pressure was >140 mm Hg or <40 mm Hg; 5) heart rate was >150 beats·minute$^{-1}$

or <40 beats·minute$^{-1}$; 6) systolic and diastolic blood pressure deviated ±50 mm Hg and ±20 mm Hg, respectively from surrounding values; and/or 7) heart rate deviated ±30 beats·minute$^{-1}$ from the surrounding values. Ambulatory blood pressure data was averaged during the baseline period and for the last 40 minutes of the rest periods between each short session of physical activity.

**Holter Monitoring**

**Paragraph Number 16** The Aria Digital Recorder (Del Mar Reynolds Medical, Inc., Irvine, CA) was used to observe sympathetic modulation through power spectral analysis of heart rate variability. The EKG was analyzed for the baseline period and the post-treatment period following each short session of physical activity. The data from Aria Digital Recorder was scanned on a computer-assisted Holter system (Impresario, Solo Holter analysis software, Del Mar Reynolds Medical, Inc., Irvine, CA) for variables of heart rate variability. Manual editing of the R-R interval data was performed to ensure correct identification and classification of every QRS complex (22). Artifact and ectopic beats were removed for the R-R interval calculation. The data was then used for the power spectral analysis of heart rate variability.

**Paragraph Number 17** Frequency-domain measures of heart rate variability were assessed using the fast Fourier transform. The total power was calculated by the standard deviation of the R-R interval (<0.1 Hz). Heart rate variability of the total nominal record was computed using the whole range of high frequency

power (0.15-0.40 Hz), low frequency power (0.04-0.15 Hz), and very low frequency power (0.003-0.04 Hz). Normalized (%) values were calculated. Normalized units represent the relative value of each power component in proportion to the total power minus the very low frequency component. The ratio of low frequency power to high frequency power was determined. Normalized low frequency power, high frequency power, and the ratio of low to high frequency were averaged for the baseline period and for the last 40 minutes of the rest periods between each short session of physical activity.

### *STATISTICAL METHODS*

**Paragraph Number 18** Data was expressed as means ± standard error of the mean (SE). Statistical analyses were performed by use of descriptive statistics, and analysis of variance (ANOVA) with repeated measures. Paired t-test was used for post hoc comparisons. Descriptive statistics were performed to describe the characteristics of subjects. The variables were sex, age, body mass index (BMI), screening systolic and diastolic blood pressures, and $VO_2$peak. One-way ANOVA with repeated measures was used to test if the variables of blood pressure and sympathetic modulation differed over time. Tukey test was used for post-hoc comparisons. The level of significance was set at $p<0.05$. The SPSS software (SPSS 13.0) was used for all statistical analyses.

## *RESULTS*

### Subjects

**Paragraph Number 19** Twenty six adults were screened for the study; five were found to be ineligible during the blood pressure screening process; four have normal blood pressure and one has hypertension. Twenty one adults with prehypertension who were qualified based on screening blood pressure participated in the study. One participant did not complete the study because of time constraints. Twenty adults with prehypertension completed the study. Demographics of the subjects are summarized in Table 1.

### Exercise Stimulus

**Paragraph Number 20** The 20 participants who completed the study performed a maximal voluntary effort on the exercise test as verified by reaching 107.7±1.3% predicted maximal heart rate (220-age). The intensity of physical activity was 51.9±0.6% of $VO_2$peak.

### Blood Pressure Reduction

**Paragraph Number 21** The average ambulatory blood pressures for three rest periods are illustrated in Figure 2. The beginning times for the analyses of the ambulatory measurements were 9:00 ± 0:03 for baseline, 9:42 ± 0:04 following the first short session, 10:41 ± 0:03 following the second short session and 11:42 ± 0:04 following the third short session. The number of ambulatory blood pressure measurements was three in the baseline period and six in the rest

period following each short sessions of physical activity treatment. The average blood pressures for baseline and rest periods are listed in Table 2.

**Paragraph Number 22** The average baseline blood pressures and average blood pressures for the rest periods following each short physical activity session was analyzed by one-way ANOVA with repeated measures. A significant main effect was found in systolic blood pressure ($p=0.039$) while no main effect was found in diastolic blood pressure ($p=0.630$). Further analyses revealed that systolic blood pressure was significantly decreased following the third short session ($-4.0 \pm 1.7$ mm Hg) compared to each session.

### Sympathetic Modulation

**Paragraph Number 23** Sympathetic modulation measured by heart rate variability was averaged for baseline and for the rest periods following each short physical activity session. The values of normalized high frequency power, normalized low frequency power, and the ratio of low to high frequency power are summarized in Table 3. No significance was found in any of these variables of heart rate variability.

## *DISCUSSION*

**Paragraph Number 24** The purpose of the study was 1) to investigate the blood pressure reduction during the rest periods following each successive short session within the accumulation of physical activity over a 3-hour period in adults

with prehypertension, and 2) to study sympathetic modulation during the rest periods following each short physical activity session over a 3-hour period in adults with prehypertension. We hypothesized 1) the systolic and diastolic blood pressures following each successive short physical activity session would be lower than the blood pressure of previous sessions in adults with prehypertension, and 2) the sympathetic modulation, measured by power spectral analysis of the heart rate variability, would be different following each successive short physical activity session in adults with prehypertension. Our study is the first one to examine the blood pressure response during the rest periods between several short sessions in the accumulation of physical activity as a treatment for prehypertension.

**Paragraph Number 25** In 2003, 45 million adults with prehypertension (5) were added to the patient population in need of treatment for high blood pressure; which represents 31% of the US population (26). Lifestyle modification (2, 5), including regular physical activity, is the only recommended treatment for prehypertension. It is also the only recommended treatment for the prevention of prehypertension progressing to hypertension (27). Yet, supporting literature on regular physical activity as a treatment for prehypertension is limited (6). Thus, our focus on adult with prehypertension was warranted.

**Paragraph Number 26** The physical activity stimulus we presented to the subjects was effective in lowering systolic and diastolic blood pressures which

was associated with increased parasympathetic and decreased sympathetic activity. As a result of 4 x 10-minute sessions of physical activity over a four hour period (19), systolic blood pressure decreased 5.4 ± 1.7 mmHg for 11 hours; diastolic blood pressure decreased 3.4 ± 1.3 mmHg for 10 hours. Furthermore, the differences in normalized low frequency power ($r=0.517$, $P<0.01$) and high frequency power ($r=-0.503$, $P<0.05$) were correlated with the systolic blood pressure reduction. The differences in normalized low ($r=0.745$, $P<0.001$), high frequency ($r=-0.738$, $P<0.001$), and the ratio of low to high frequency ($r=0.756$, $P<0.001$) were correlated with the diastolic blood pressure reduction. In the present study we found a difference in systolic blood pressure over time using ANOVA with repeated measures, whereas no difference in diastolic blood pressure was found. Tukey post-hoc comparison indicated a significant reduction in systolic blood pressure following the third session. The accumulation of the first two sessions was not a sufficient stimulus to induce a statistically significant blood pressure reduction; however, the addition of the third session decreased systolic blood pressure. Thus, it clearly demonstrates an additive effect of successive sessions on blood pressure reduction. Furthermore, the reductions in blood pressure following the accumulation of physical activity that we observed in our previous studies (17, 19) might be due to this additive effect of successive sessions. There was no relationship between the reduction in systolic blood pressure during the rest periods and the resultant blood pressure reduction, however.

**Paragraph Number 27** Our finding in blood pressure reduction was different from other studies investigating the rest periods between each short session (1, 10). Other investigators (1, 10) who observed the rest periods between successive sessions of exercise found similar responses between two sessions. In these studies (1, 10), EPOC was studied during the rest periods following two short sessions vs. one long session. Kaminsky et al. (10) investigated EPOC following a 50-minute exercise session compared to two 25-minute exercise sessions at 70% $VO_2$max. The two 25-minute runs were separated by 30 minutes of sitting rest. The magnitude of EPOC was similar for the two rest periods following the short sessions; and similar to the magnitude following the continuous session. Almuzaini et al. (1) also reported the EPOC following a 30-minute exercise session to two 15-minute exercise sessions, separated by 6 hours. A 20-minute measurement of EPOC followed each short session. EPOC measurements following two short sessions were not different from each other and were not different from the EPOC following the continuous session. Although both Kaminsky et al. and Almuzaini et al. found no additive effect in EPOC between the rest periods of the short sessions (1, 10), we found the additive effect of successive sessions in blood pressure reduction. This difference in successive sessions in our study might be due to the specific variable we measured, blood pressure, or due to the number of rest periods we utilized.

**Paragraph Number 28** In our study the duration of the rest period was 50 minutes and the duration of the monitoring period was the last 40 minutes of the rest period. This 50-minute rest period enabled the optimal time for ambulatory blood pressure monitoring. Had we extended the rest periods to 2-3 hours, our ambulatory monitoring following the accumulation of physical activity (19) would have been reduced 4-7 hours, compromising the ability to detect a blood pressure reduction for the entire stimulus before the subjects went to bed. The first 10 minutes of the 50 minutes was not included in the rest period data because it may have been elevated as a result of the exercise (Figure 2). Looking at our hourly data from our previous exercise studies (17, 18, 25), we found that the reduction in blood pressure for the first hour following exercise is not as great as the subsequent hours. Thus, we may have compromised our ability to detect a significant blood pressure reduction during the rest period if we had included the first 10 minutes.

**Paragraph Number 29** The mechanisms of post-exercise hypotension are not fully understood at this time; however, sympathetic modulation has recently received increased focus as a possible mechanism (9, 14). Sympathetic modulation during the 50-minute rest period did not appear to be affected by short sessions of physical activity in our study even though we found changes in systolic blood pressure. These findings are similar to those reported by Legramante and colleagues (13). They found no significant changes in sympathetic modulation although they elicited a significant 11.9 mm Hg reduction

in systolic blood pressure and a 5.3 mm Hg reduction in diastolic blood pressure. In their study (13), both post-exercise (graded exercise to 87% of predicted heart rate max) blood pressure and heart rate variability were measured for 5 minutes between 60 to 90 minutes following exercise. On the other hand, we did find that sympathetic modulation was associated with the reduction in blood pressure following the accumulation of physical activity when averaged over the 11-hour period of the systolic blood pressure reduction (19). It seemed reasonable to be able to detect a change in sympathetic modulation for the 50-minute rest period between each short session. Yet, Pober and colleagues (20) found no significant increase in parasympathetic activity at 1, 3, and 6 hours after 60 minutes of cycle ergometry at 65% of $VO_2$peak. They did, however, find a significant increase in sympathetic activity at 6 and 22 hours following the exercise. Thus, it appears as though the change in sympathetic modulation lags behind the change in early stage of post-exercise hypotension (1-2 hours following the exercise). If the lag is a true phenomenon, perhaps sympathetic modulation is not the mechanism of early stage of post-exercise hypotension.

**Paragraph Number 30** Three 10-minute walking sessions were effective in reducing systolic blood pressure in prehypertension. This immediate and favorable response associated with a few physical activity sessions may encourage the public to participate in a more active lifestyle. Furthermore, the accumulation of several 10-minute walking sessions may be more effective than continuous exercise because the multiple short sessions may promote

adherence and may fit better into a busy schedule for most Americans. In summary, successive short physical activity sessions presented an additive effect on systolic blood pressure reduction whereas they did not affect diastolic blood pressure and sympathetic modulation in adults with prehypertension. Continued investigation of the mechanisms of blood pressure reduction is warranted.

***ACKNOWELDGEMENTS***

**Paragraph Number 31** We thank our participants for their time. This study was partially funded by student research Grants-in-Aid from Gatorade Sports Science Institute, the University Graduate School, School of Health, Physical Education and Recreation, and Adult Fitness Program at Indiana University.

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***FIGURE 1.*** Study design

Figure 1

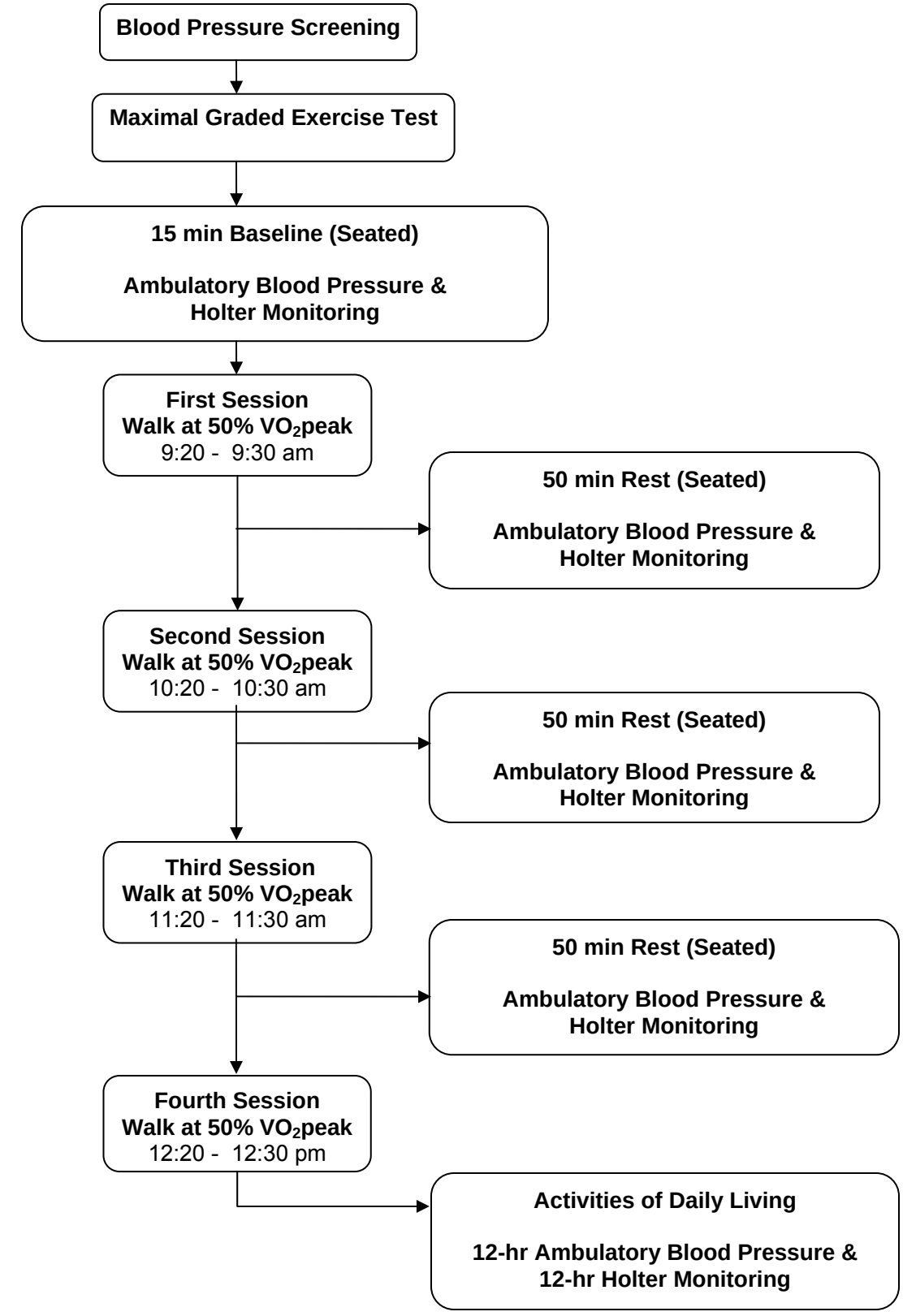

Blood Pressure Screening
Maximal Graded Exercise Test
15 min Baseline (Seated)
Ambulatory Blood Pressure &
Holter Monitoring
First Session
Walk at 50% VO2peak
9:20 - 9:30 am
50 min Rest (Seated)
Ambulatory Blood Pressure &
Holter Monitoring
Second Session
Walk at 50% VO2peak
10:20 - 10:30 am
50 min Rest (Seated)
Ambulatory Blood Pressure &
Holter Monitoring
Third Session
Walk at 50% VO2peak
11:20 - 11:30 am
50 min Rest (Seated)
Ambulatory Blood Pressure &
Holter Monitoring
Fourth Session
Walk at 50% VO2peak
12:20 - 12:30 pm
Activities of Daily Living
12-hr Ambulatory Blood Pressure &
12-hr Holter Monitoring

***FIGURE 2.*** Blood pressure during the baseline and the three rest periods following the short physical activity sessions in prehypertension. Baseline blood pressure was averaged for 15 minutes. Physical activity sessions are illustrated by shaded area. The data points following the shaded physical activity session were blood pressure in the rest periods following the short sessions. ● represents systolic blood pressure and ○ represents diastolic blood pressure. Bars represent standard errors.

Figure 2

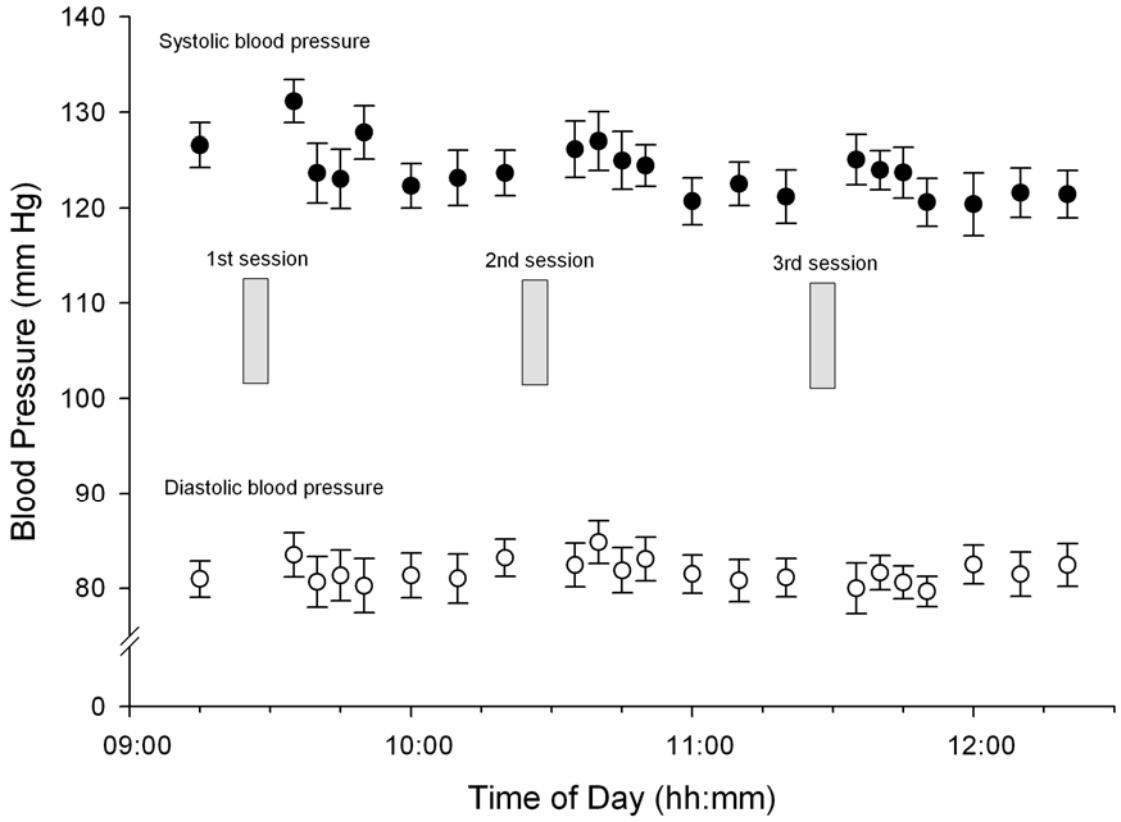

Systolic blood pressure
Diastolic blood pressure
1st session
2nd session
3rd session
Blood Pressure (mm Hg)
Time of Day (hh:mm)
140
130
120
110
100
90
80
0
09:00
10:00
11:00
12:00

***TABLE 1. DEMOGRAPHICS OF SUBJECTS***

| **Variables** | |
|---|---|
| Number | 20 |
| Sex (men/women) | 15/5 |
| Race | 18 Caucasian |
| | 2 Asian |
| Age (years) | 47.2 ± 2.9 |
| Weight (kg) | 84.5 ± 4.4 |
| Height (cm) | 176.3 ± 1.7 |
| Body mass index ($kg \cdot m^{-2}$) | 27.0 ± 1.2 |
| $VO_2$peak ($ml \cdot kg \cdot^{-1} \cdot min^{-1}$) | 34.5 ± 1.6 |
| Screening systolic blood pressure (mm Hg) | 131.9 ± 1.1 |
| Screening diastolic blood pressure (mm Hg) | 83.0 ± 1.6 |

Values were expressed as mean ± S.E.

***TABLE 2. AMBULATORY BLOOD PRESSURE***

| | ***Baseline*** | ***Rest period following the 1st Session*** | ***Rest period following the 2nd session*** | ***Rest period following the 3rd session*** |
|---|---|---|---|---|
| **Systolic Blood Pressure (mmHg)** | 126.6 ± 2.4 | 123.9 ± 2.5 | 123.5 ± 2.3 | 122.6 ± 2.4* |
| **Diastolic Blood Pressure (mmHg)** | 81.0 ± 1.9 | 81.2 ± 2.4 | 82.3 ± 1.9 | 81.6 ± 1.7 |

Values of blood pressure were averaged for the 15-minute baseline period and the last 40 minutes of the rest period following short physical activity sessions. Values were expressed as mean ± S.E.

* denotes significant differences from baseline blood pressure at $p<0.05$.

***TABLE 3. SYMPATHETIC MODULATION BY HEART RATE VARIABILITY***

| | ***Baseline*** | ***Rest period following the 1st session*** | ***Rest period following the 2nd session*** | ***Rest period following the 3rd session*** |
|---|---|---|---|---|
| **Normalized low Frequency power (%)** | 80.0 ± 1.3 | 80.1 ± 2.3 | 80.1 ± 2.6 | 78.6 ± 3.4 |
| **Normalized high frequency power (%)** | 17.9 ± 1.1 | 17.8 ± 2.1 | 17.8 ± 2.3 | 19.1 ± 3.1 |
| **Ratio of low to high frequency** | 4.9 ± 0.4 | 6.0 ± 0.8 | 6.3 ± 0.9 | 6.7 ± 1.0 |

Values of heart rate variability were averaged for the 15-minute baseline period and the last 40 minutes of the rest period following short physical activity sessions.

Values were expressed as mean ± S.E.

# APPENDICES

## *APPENDIX A – REVIEW OF THE LITERATURE*

The purpose of this study is (1) to compare the blood pressure reduction following the accumulation of short bouts of exercise and one long bout of exercise in adults with prehypertension, and (2) to compare the blood pressure reduction following each successive short bout of exercise in adults with prehypertension. In addition, sympathetic modulation will be investigated as a possible mechanism for the blood pressure reduction following exercise in adults with prehypertension. The literature related to this study is reviewed in this amendment under the following topics: (a) Hypertension-A Serious Public Health Problem; (b) Regulation of Blood Pressure; (c) Etiology of Hypertension; (d) Treatment and Prevention of Hypertension; (e) Accumulation of Exercise on Blood Pressure Reduction; (f) Post Exercise Hypotension, (g) Power Spectral Analysis of Heart Rate Variability; (h) Ambulatory Blood Pressure Monitoring, (i) Physical Activity Monitoring, and (j) Summary.

## *HYPERTENSION- A SERIOUS PUBLIC HEALTH PROBLEM*

High blood pressure, or hypertension is a major risk factor for stroke (78), coronary artery disease (78), congestive heart failure (135), and end-stage renal disease (64). Approximately 50 million individuals in the United States (U.S.) diagnosed with hypertension (defined as a systolic blood pressure ≥140 mm Hg, a diastolic blood pressure ≥90 mm Hg or current treatment with antihypertensive medication) (13). In the U.S., the prevalence of hypertension has increased by 13.1% in the last decade (43). The estimated annual direct and indirect costs of

hypertension are 55.5 billion dollars in the U.S.(5). The risk of developing this costly disease increases with advancing age.

Lifetime risk of developing hypertension is 90% in individuals with normal blood pressure (<140 mm Hg systolic or <90 mm Hg diastolic) at 55 to 65 years of age (133). Moreover, the risk of cardiovascular disease associated blood pressure begins as low as 115 mm Hg systolic blood pressure. Suboptimal systolic blood pressure (>115 mm Hg) is responsible for 62% of cerebrovascular disease (i.e., stroke), 49% of ischemic heart disease, and is the primary attributable risk for death throughout the world (146). In addition, there is a two-fold increase in relative risk from cardiovascular disease with systolic blood pressure of 130 to 135 mm Hg and with diastolic blood pressure of 85 to 89 mm Hg compared with a blood pressure of 120/80 mm Hg. Thus, emphasis has been made to lower blood pressure to prevent hypertension and to reduce the risk of cardiovascular disease.

**Classification of Blood Pressure**

The 7$^{th}$ Report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure, or the JNC 7 (14), has provided a new blood pressure classification system for adults aged 18 years or older. This system is summarized in Table 1. The classification of blood pressure is based on the mean of two or more properly measured seated blood pressure readings on each of two or more office visits. In the JNC7 report, a new category designated prehypertension has been added. This new classification of

hypertension has been introduced to identify those individuals in whom early intervention by adopting healthy lifestyle would lead to reduce blood pressure and to decrease the rate of progression of hypertension or to prevent hypertension entirely. Another change in classification from the 6th Report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure is to combine stage two and three hypertension.

**Table 1. Classification of blood pressure for adults aged 18 years or older***

| ***Classification*** | ***Systolic Blood Pressure (mm Hg)*** | | ***Diastolic Blood Pressure (mm Hg)*** |
|---|---|---|---|
| **Normal** | <120 | and | <80 |
| **Prehypertension** | 120-139 | or | 80-89 |
| **Hypertension (Stage 1)** | 140-159 | or | 90-99 |
| **Hypertension (Stage 2)** | >160 | or | >100 |

*Based on the mean of two or more properly-measured seated blood pressure readings on each of two or more physician office visits.

From the 7th Report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure, JNC 7 (2003) (14)

Historically, a greater emphasis has been placed on diastolic than systolic blood pressure as a predictor of cerebrovascular and coronary heart disease (24). Indeed, until the 1990s, diastolic blood pressure was used as an inclusion criterion in hypertension studies (19), while subjects with isolated systolic hypertension were excluded from such studies. It is currently emphasized that a systolic blood pressure >140 mm Hg is a much more important cardiovascular disease risk factor than diastolic blood pressure in individuals older than 50 years (59, 120).

In summary, hypertension is an important risk factor for cardiovascular disease. The prevalence of hypertension increases with advancing age. The risk of cardiovascular disease begins blood pressure as low as 115/75 mm Hg. Thus, the prevention and treatment of hypertension are major public health challenge for society.

## *REGULATION OF BLOOD PRESSURE*

The regulation of blood pressure is traditionally described in terms of homeostasis. Homeostasis indicates blood pressure continuously perturbed by external stimuli although it always displays the tendency to return to a reference set point. There are a number of systems involved in the regulation of blood pressure. The primary factors include the autonomic nervous system for the short-term blood pressure regulation and the kidneys for the long-term blood pressure regulation.

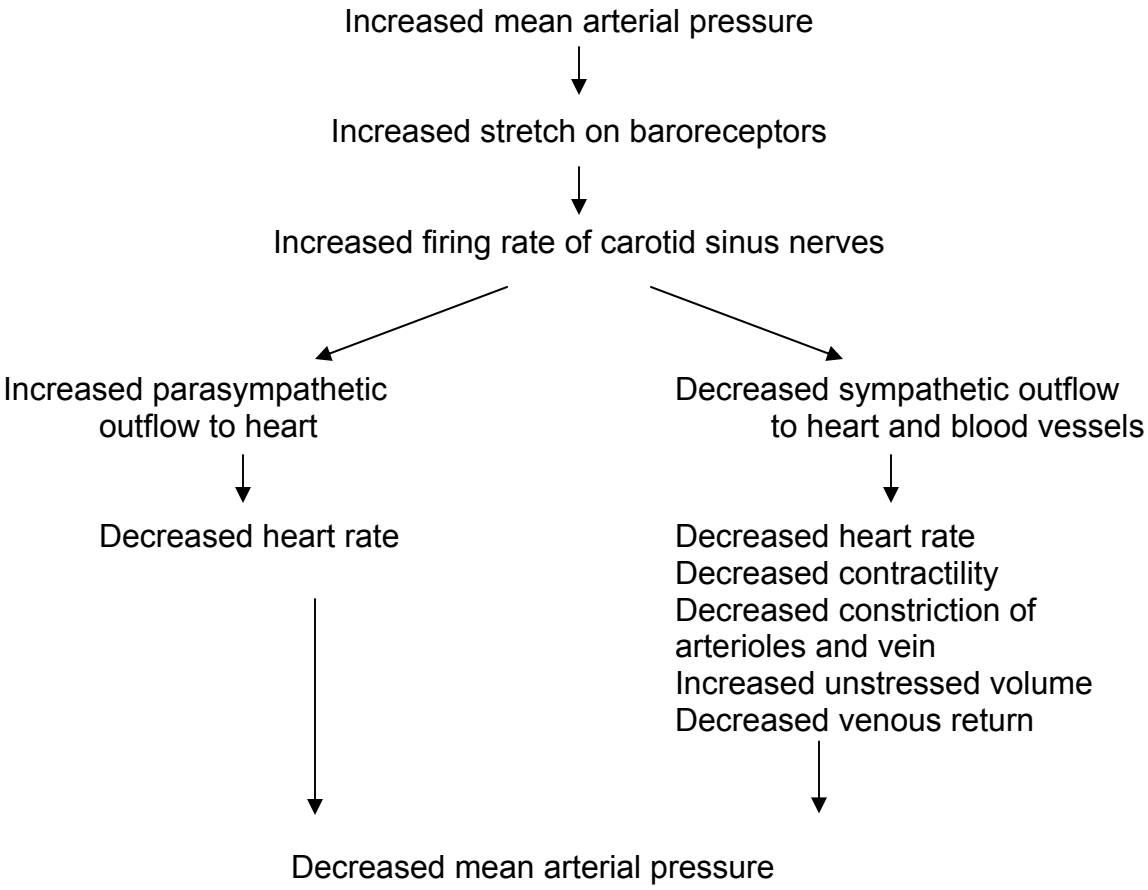
## Role of Autonomic Nervous System in Short-Term Blood Pressure Regulation

One of the most important functions of the autonomic nervous system in the circulation is its capability to cause rapid alterations in blood pressure. The entire vasoconstrictor and cardioaccelerator functions of the sympathetic nervous system are stimulated as a unit. At the same time, there is reciprocal inhibition of the parasympathetic vagal inhibitory signals to the heart. These responses can be found in 1) baroreceptor reflexes, 2) chemoreceptor reflexes, 3) atrial and pulmonary reflexes, and 4) central nervous system ischemic response.

1) Baroreceptor Reflex

The baroreceptor reflex is the most well known mechanism for the regulation of blood pressure. This is a classic negative feedback reflex system. Baroreceptors are nerve endings lying in the walls of the arteries. A few baroreceptors are located in the wall of almost every large artery of the thoracic and neck regions. But, baroreceptors are abundant in the wall of the carotid sinus and the wall of the aortic arch. The baroreceptor reflex regulates instantaneous blood pressure fluctuation such as seen in postural changes. The baroreceptor reflex is also an important response to acute blood loss (e.g., hemorrhage). The regulations of blood pressure involving baroreceptor reflex are described in Figure 1.

*Figure 1. Baroreceptor reflex in regulation of blood pressure*



In resting conditions muscle sympathetic nerve activity is under strong regulation by the arterial baroreceptor and cardiopulmonary receptor reflexes. During exercise, the baroreceptor reflex is reset to a higher operating point and sympathetic activity is increased (84, 137). After exercise, these reflexes are reset to lower pressures such that sympathetic outflow from the central nervous system is lower than pre-exercise pressure. In established hypertension, the baroreceptor reflex is reset to maintain elevated blood pressures. This resetting is caused by interactions with higher nervous center and humoral factors such as angiotensin II (148).

2) Chemoreceptor Reflex

Closely associated with the baroreceptor reflex is a chemoreceptor reflex that is also involved in blood pressure regulation. The chemoreceptors are chemosensitive cells sensitive to decrease the partial pressure of oxygen (Po2), increased the partial pressure of carbon dioxide (Pco2), or increased concentration of hydrogen ion. The chemoreceptors excite nerve fibers that pass along adjacent to the baroreceptor fibers through Hering's nerves and the vagus nerves into the vasomotor center.

Chemoreceptors are in close contact with the arterial blood flow. When arterial blood pressure falls below a critical point, the chemoreceptors are stimulated by the decreased Po2 and increased Pco2. The signals transmitted from the chemoreceptors into the vasomotor center excite the vasomotor center to elevate the blood pressure. The chemoreceptor reflex is, however, not a

powerful regulator due to the fact that the chemoreceptors are not stimulated strongly until the arterial blood pressure falls below 80 mm Hg (37, 45).

3) Atrial and Pulmonary Artery Reflexes

Both the atria and the pulmonary arteries have stretch receptors, or low pressure receptors. These low pressure receptors play an important role to minimize arterial pressure changes in response to changes in blood volume. They elicit reflexes parallel to the baroreceptor reflexes to make the total reflex system much more potent for the regulation of blood pressure (37).

Stretch of the atria also causes reflex dilation of the afferent arterioles in the kidneys. Signals are transmitted simultaneously to the hypothalamus to decrease the secretion of anti-diuretic hormone. The decreased afferent arteriolar resistance causes the glomerular capillary pressure to rise, with resultant increase in filtration of fluid into the kidney tubules. The diminution of anti-diuretic hormone attenuates the reabsorption of water from the tubules. Thus, urine output is increased and blood volume is regulated (37).

4) Central Nervous System Ischemic Response

Most nervous regulation of blood pressure is achieved by reflexes originating in the baroreceptors, the chemoreceptors, and the low pressure receptor, all of which are located in the peripheral circulation. In cerebral ischemia the neurons in the vasomotor center itself respond directly to the ischemia and become excited. This blood pressure elevation in response to

cerebral ischemia is known as the central nervous system ischemic response. This ischemic response does not become very active until the arterial blood pressure falls below 60 mm Hg (37).

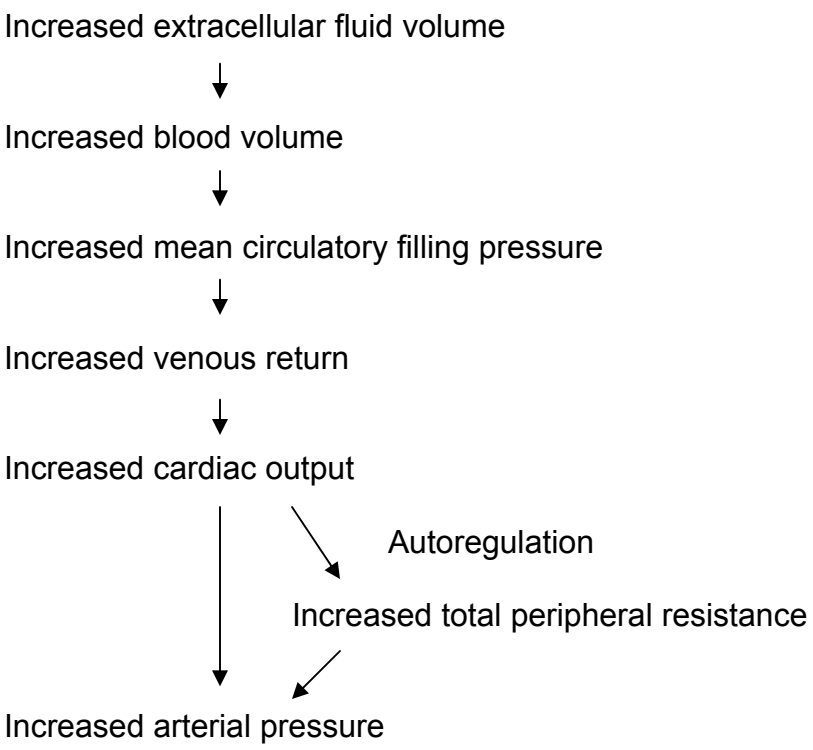
**The Role of the Kidneys in Long-Term Blood Pressure Regulation**

In the long-term regulation of blood pressure, the kidneys work through two mechanism: 1) Renal-volume control system and 2) Renin-angiotensin system.

1) Renal-Volume Control System

Blood pressure rises when the body retains too much extracellular fluid (see Figure 2). The rising pressure has a direct effect to cause the kidney to excrete the excess extracelluar fluid. This phenomenon is called pressure diuresis (or pressure natruresis). Pressure diuresis represents the ability of the kidneys to respond to changes in blood pressure by altering the renal excretion of salt and water. At an arterial blood pressure of 50 mm Hg, the urinary output is zero. At 100 mm Hg, it is normal and at 200 mm Hg it is about six to eight times normal.

*Figure 2. The sequential steps of the regulation of blood pressure in relation to extracellular fluid*

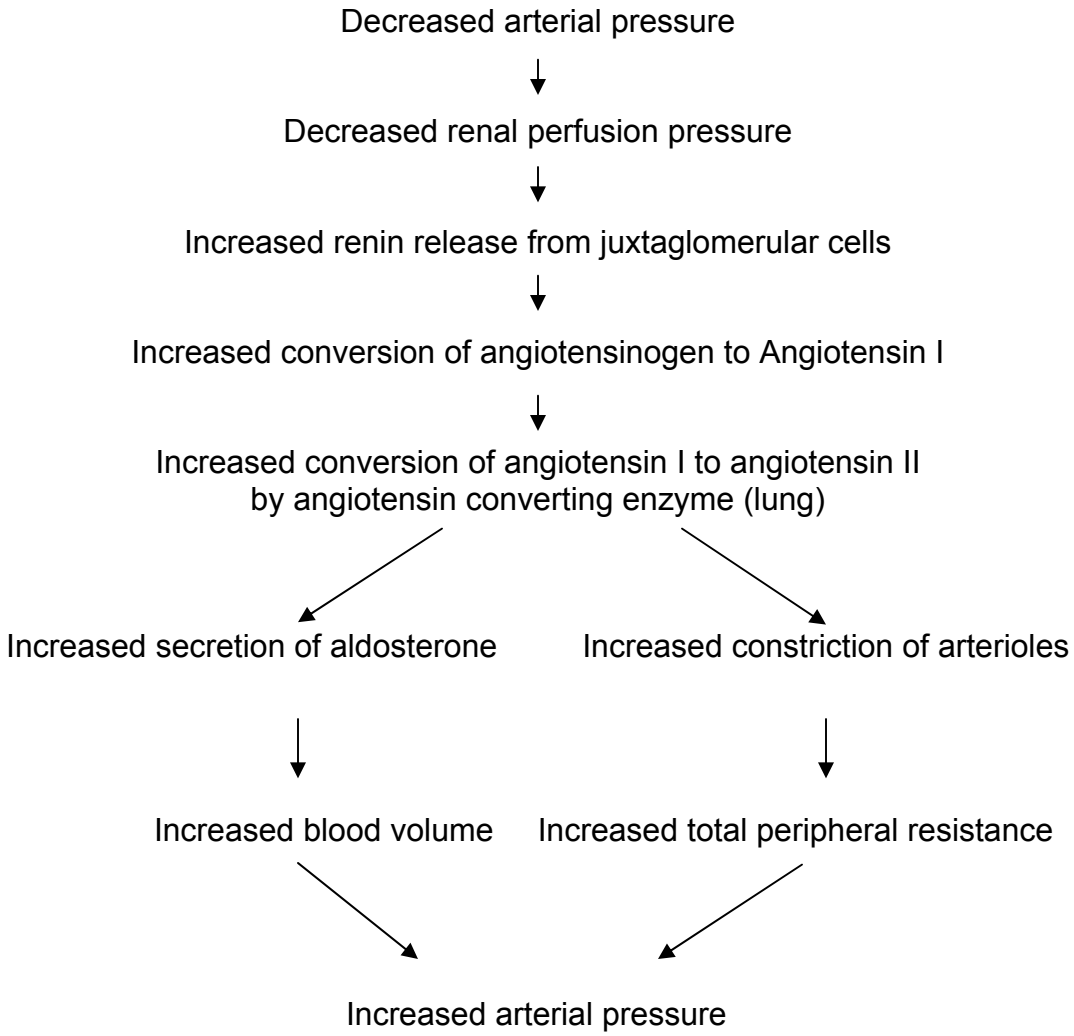



The two determinants of the renal-volume control system are 1) renal output of salt and water, and 2) salt and water intake (38). When the net intake of water and salt (defined as the intake minus the nonrenal output such as sweat) exactly equals renal output urinary output of both water and salt remains normal, and the arterial pressure is normalized. When arterial blood pressure falls below the normalized point, the decreased pressure has a direct effect on the kidneys to reduce the urinary output of water and salt.

2) Renin-Angiotensin System

The kidneys regulate blood pressure not only through changes in extracellular fluid volume but also through the renin-angiotensin system. The renin-angiotensin system was first discovered and described in the 1930's. This system, unlike the baroreceptor reflex, represents a slow response. Complexity of the renin-angiotensin allows multiple options of treatment for hypertension. The renin-angiotensin system (see Figure 3) primarily adjusts blood volume. The kidney plays a major role in the renin-angiotensin system. The initiating step is the release of renin. The three factors controlling renin release are 1) the afferent arteriole blood pressure in the juxtaglomerular apparatus, 2) $Na^+$ and $Cl^-$ concentrations in the macula densa, and 3) increased sympathetic drive to granular cells respectively. The result of each is an increase in renin. The renin, in turn, stimulates the increase in angiotensin II. Angiotensin II stimulates constriction of arterioles throughout the systemic circulation. It also stimulates release of aldosterone from the adrenal cortex (zona glomerulosa), increasing salt and water retention and blood volume. It also turns on the adrenal medulla, releasing epinephrine and norepenephrine.

*Figure 3. Renin-angiotensin system in regulation of blood pressure*



In summary, there are a number of systems involved in the regulation of blood pressure. The autonomic nervous system is involved in the short-term blood pressure regulation and the kidneys are involved in the long-term blood pressure regulation. Physiological and clinical significance of each identified factor is not entirely clear.

## *ETIOLOGY OF HYPERTENSION*

Primary (essential or idiopathic) hypertension accounts for 90-95% of all cases of hypertension. Primary hypertension is defined as high blood pressure in which secondary causes such as chronic kidney disease, drug induced/related hypertension, primary aldosteronism, Cushing's syndrome or steroid therapy, pheochromocytoma, coarctation of the aorta, and/or thyroid/parathyroid disease are not present.

### Primary Hypertension (essential or idiopathic hypertension)

Hypertension can develop in response to an increase in cardiac output and/or a rise in total peripheral resistance. The interplay of various factors affecting cardiac output and/or total peripheral resistance may precipitate hypertension. These factors include 1) genetic predisposition, 2) increased sympathetic nervous activity, and 3) obesity.

1) Genetic Predisposition (30-60%)

Hypertension is a multigenetic disease. In particular, the renin-angiotensin genes play an important role in the pathogenesis of hypertension. Upregulation of the transcription of angiotensinogen, and angiotensin-converting enzyme genes increases blood pressure through the increased concentration of angiotensin II (53, 67). Other candidate genes, such as angiotensin II type 1 receptor, endothelins, atrial natriuretic peptide, renin, e-NOS, insulin receptor, and low density lipoprotein receptor have been reported to play a role in pathogenesis of human hypertension (53).

2) Increased Sympathetic Nervous Activity

In early hypertension there is a state of increased cardiac output via increased stroke volume and heart rate. This state is, in part, neurogenic because of its normalization after pharmacological blockade of the autonomic nervous system. This state is gradually transferred into the cardiovascular pattern of normal cardiac output and elevated total peripheral resistance. The conversion from a high to normal cardiac output is secondary to decreased cardiac compliance and beta-adrenergic responsiveness.

Sympathetic activity is frequently activated, at least in early stages in primary hypertension. Evidence was supported by the elevated spillover of norepinephrine from sympathetic neuroeffector junction, and direct measurements of sympathetic nerve activity. The increased spillover was evident in the heart, kidney, and subcortical region of the forebrain, which would

explain the hemodynamic characteristics of early hypertension, increased heart rate, cardiac output and renal vascular resistance.

Sympathetic nervous system has been investigated for the long-term regulation of blood pressure (38). The kidney itself can be controlled by other factors such as neural and humoral factors. The renal sympathetic nerves can promote anti-natruresis and can affect renal-volume control system directly through renal tubular innervation and indirectly by neurally mediated increases in renin release and renal vascular resistance (72).

It has been documented that hypertensive adults have more frequent neurovascular compression (NVC) of the rostral ventrolateral medulla, which is the major center of the sympathetic nervous system regulating the cardiovascular system. In its early stage, hypertension is accompanied by sympathetic activation, then sympatho-renal interactions in conjunction with genetic and environment factors and the tropic effects on vascular muscle may play important roles in the long-term regulation of arterial pressure.

3) Obesity

Obesity, and especially abdominal obesity, is associated with the development of hypertension. In the Framingham study, each 10% weight gain is associated with a 6.5 mm Hg increase in systolic blood pressure (7). The relation between blood pressure and body weight is not restricted to morbid obesity, but is continuous throughout the range of body weight (40). The

mechanisms underlying the association between obesity and hypertension are not fully understood.

In obesity, alterations in intrarenal vasoactive substances would be a factor contributing to the development of hypertension, and the disturbed insulin sensitivity could impair myogenic response of preglomerular vessels. Insulin stimulates nitric oxide production in the endothelium. Impaired nitric oxide production would lead to increased vascular tone and hypertension. Cellular hypertrophy or mitogen-activated protein (MAP) kinases and NAD(P)H oxidases produce reactive oxidative stress. Angiotensin II increases vascular superoxide anion production by activation of membrane-bound NAD(P)H oxidase. Increased vascular superoxide anion production can lead to reduced bioavailability of nitric oxide and impaired endothelium-dependent relaxation, a characteristic of disease states such as hypertension (32).

The etiology of primary hypertension is not fully understood yet. There are many factors associated with hypertension. In this review, genetic predisposition, increased sympathetic nervous activity, and obesity are discussed as major factors contributing to the development of hypertension.

## *TREATMENT AND PREVENTION OF HYPERTENSION*

### Treatment of Hypertension

The primary goal of treatment of hypertension is to achieve the maximum reduction in the total risk of cardiovascular morbidity and mortality (14, 15, 24, 145). It is also recommended that blood pressure be treated below 140/90

mmHg or below 130/80 mmHg in patients with diabetes or chronic kidney disease. Treatments of hypertension include 1) lifestyle modifications and 2) pharmacological treatment.

1) Lifestyle Modifications

Several health organizations recommend the use of lifestyle modifications as the primary and adjunctive treatment for hypertension (15, 24, 143, 145). There are minimal cost and side effects associated with lifestyle modifications. Major lifestyle modifications recommended to lower blood pressure include weight reduction, diet, exercise, and moderation of alcohol consumption (see Table 2). Multiple lifestyle modifications can achieve better results to reduce blood pressure and cardiovascular risk (147).

*Table 2. Lifestyle medications to manage hypertension*

| Modification | Recommendation | Approximate Systolic BP Reduction |
|---|---|---|
| **Weight Reduction** | Maintain normal body weight (BMI 18.5-24.9 kg/$m^2$) | 5-20 mm Hg/10 kg |
| **Adopt DASH Eating Plan** | Consume a diet rich in fruits, vegetables, and low fat dairy products with reduced content of saturated and total fat | 8-14 mm Hg |
| **Dietary Sodium Reduction** | Reduced <100mmol/day (2.4g sodium or 6g sodium chloride | 2-8 mm Hg |
| **Physical Activity** | Engage in regular aerobic physical activity (at least 30 min per day, most of days of the week) | 4-9 mm Hg |
| **Moderation of Alcohol Consumption** | Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol;eg, Men: <2 drinks/day; women and lighter weight 24 oz beer, 10 oz wine, or 3oz 80 proof whiskey)) in most men and no more than 1 drink per day in women and lighter-weight person | 2-4 mm Hg |

Table 2 modified from JNC7 (14). BMI: body mass index, BP: blood pressure, DASH: Dietary Approaches to Stop Hypertension

In this review, exercise, a lifestyle modification, is further discussed. Exercise is an integral component of lifestyle modifications for treatment of hypertension (4) because exercise reduces blood pressure and decreases cardiovascular mortality independent of blood pressure and other risk factors (112). For example, normotensive and hypertensive individuals also improve plasma lipoprotein-lipid profiles and improve insulin sensitivity with exercise training (42). The exercise prescription for treatment of hypertension is composed of more than 30 minutes of continuous or accumulated endurance physical activity (40 to 60% of maximal oxygen uptake, $VO_2$max) on most, preferably all, days of the week (4, 15). The magnitude of blood pressure reductions resulted from aerobic exercise training is related to baseline blood pressure (26). In other words, the decrease in blood pressure appears to be more pronounced in hypertensive (4.94 mm Hg in systolic and 3.73 mm Hg in diastolic blood pressure) than in normotensive (4.04 mm Hg in systolic and 2.33 mm Hg in diastolic blood pressure)individuals (142). The blood pressure reduction following aerobic exercise training in hypertensive adults is independent of weight loss (138, 142). Resistance exercise is not the recommended mode to control blood pressure due to a pressor effect (138).

2) Pharmacological Treatment

In this review, pharmacological treatment for hypertension is briefly summarized. Several classes of medications have been shown to reduce blood pressure as well as the complications of hypertension. The classes of

antihypertensive medications are (1) angiotensin-converting enzyme inhibitors, (2) angiotensin-receptor blockers, (3) calcium channel blockers, (4) drugs with central and peripheral sympatholitic actions, (5) arteriolar dilators, and (6) thiazide-type diuretics. Based on recommendations of drug therapy made by the JNC 7, the initial drug choices for stage one hypertensive adults without compelling indications are thiazide-type diuretics. Angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta blockers, or calcium channel blockers, and/or combination may be considered. For stage two hypertensive adults two drug combinations for most (usually thiazide-type diuretic and other antihypertensive medications).

**Prevention of Hypertension**

Prevention of hypertension is imperative because the lifetime risk of developing hypertension is very high in the U.S (15). Despite the effort to control hypertension, only 31% of individuals with hypertension in the U.S. have the disease under control (i.e., with a systolic blood pressure <140 mm Hg and a diastolic blood pressure <90 mm Hg) (43). The treatment of hypertension alone might be scarce due to adverse drug effects, and lack of awareness and management of hypertension (117). Thus, prevention of hypertension becomes an important goal in overall efforts to control blood pressure and to reduce the incidence of cardiovascular diseases associated with hypertension (117, 134, 141).

The relationship between cardiovascular disease and blood pressure is strong, independent and continuous. Beginning at 115 mm Hg systolic and 75 mm Hg diastolic blood pressure the mortality from both ischemic heart disease and stroke is doubled with each increment of 20 mm Hg in systolic or 10 mm Hg in diastolic blood pressure (71). Therefore, prehypertension has been introduced to prevent hypertension and cardiovascular disease entirely (15). A small decrement in systolic blood pressure is likely to result in a substantial reduction in the blood pressure related cardiovascular disease. It has been estimated 5 mm Hg systolic blood pressure reduction would result in a 14% overall reduction in mortality due to stroke, a 9% reduction in mortality due to coronary heart disease and a 7% decrease in all-cause mortality (141).

There are several identified factors underlying hypertension including non-modifiable factors such as age, gender, and race, as well as modifiable factors including overweight, physical inactivity, excess alcohol intake, and inadequate intake of fruits and vegetables. Lifestyle modifications (see Table 2) have been primary recommended to prevent hypertension (15, 117, 141). In this review, exercise is further discussed. Exercise has been advocated as an important component for prevention of hypertension (4, 15) but has limited supporting evidence. Exercise as a means to prevent hypertension has been formulated based on epidemiological evidence (10, 91) and a few clinical studies (25, 142). Epidemiologic studies suggest an inverse relationship between physical activity or fitness and blood pressure (10, 91). Aerobic exercise training has been shown to reduce blood pressure for normotensive individuals (10, 91). Clinical studies

are warranted to investigate the effects of exercise on prevention of hypertension for individuals with prehypertension.

### *ACCUMULATION OF EXERCISE ON BLOOD PRESSURE REDUCTION*

Exercise has been advocated as an important component for the prevention and treatment of hypertension (4, 15). Indeed, physical inactivity is an independent risk factor for hypertension and cardiovascular disease.(97). Trends toward participation of exercise, however, appear to be stabilizing or diminishing, as the adherence rate of exercise programs is only 50% (21, 107). Since the most often-cited reason for not adhering to an exercise program is the lack of time (73), the accumulation of moderate physical activity, on most if not all days of the week, has been recommended as the exercise treatment for hypertension as well as prevention (4, 15). Despite these recommendations being made, there is a lack of evidence supporting the effectiveness of the accumulation of physical activity on the prevention as well as treatment of hypertension.

Physical activity is defined as any bodily movement that is produced by skeletal muscle contraction and that substantially increases energy expenditure (130). Exercise, as a subset of physical activity (130), is planned, structured and repetitive bodily movement done to improve or maintain one ore more components of physical fitness. In this review, the terms exercise and physical activity will be used interchangeably. The accumulation of physical activity has been advocated as an important component for the prevention of hypertension. There is lack of the clinical trials supporting the effectiveness of accumulating

physical activity on prehypertension. Only one study to date has demonstrated this recommendation may also be a treatment for hypertension (85).

Moreau et al. (85) found a reduction in systolic blood pressure following 12 weeks (by 6 mm Hg) and 24 weeks (by another 5 mm Hg) of a walking program (3 km/day) in 24 post-menopausal women with prehypertension and stage 1 hypertension. However, they did not report exercise intensity and duration, and it was not reported whether the 3 km was walked all at once or accumulated over a number of walking bouts throughout the day. Thus, the effect of accumulation of physical activity compared to a single long bout of physical activity on blood pressure reduction could not be determined from this study. This issue has been systemically reviewed by Hardman (47).

The accumulation of physical activity has been investigated by fractionation of exercise. Fractionation of exercise is used to investigate 1) different patterns (one continuous or long versus several short bouts of exercise with the same total duration), and 2) different intensities of exercise (moderate/hard versus low intensity of exercise) with the similar energy expenditure. Hardman (47) evaluated evidence comparing the effects of fractionation of exercise on health outcome. While it appears that fractionated exercise improves functional capacity ($VO_2$max) (47), there is little information on the effects of fractionated exercise on other health outcomes including blood pressure. Hardman recommends that further research is warranted in fractionated exercise on health outcome (47).

Many studies have compared the effects of a single bout of exercise to those of multiple bouts of exercise on parameters of health and fitness, such as $VO_2$max (2, 62), blood lipids (35), glucose/insulin dynamics , bone mass (110), and exercise adherence (113). For example, Kaminsky et al. (62) and Almuzaini et al. (2) found that the acute effects of two short bouts of exercise on excess post-exercise oxygen consumption were greater than those of one long bout of exercise. In addition, Gill et al. (35) and Murphy et al. (87) found that several short bouts of exercise were as effective as one long bout of exercise on postprandial lipidemia. However, no studies have compared the effects of single-bout exercise to fractionated exercise on blood pressure as a major outcome.

Blood pressure was reported in fractionated exercise study by Murphy and Hardman (86) as a secondary outcome. They investigated training effects of short and long bouts of brisk walking in sedentary women. Women were randomly assigned to three 10 minute walks (n=12), one 30minute walk (n=12) at 70 to 80 % of maximal heart rate for 10 weeks or control group (no walk, n=10). Pre- and post-exercise training blood pressures were measured. Although the short bouts of exercise group reduced blood pressure by 7.4 ± 7.3 mm Hg, while the long bout exercise group reduced blood pressure by 4.6 ± 5.9 mm Hg, the difference between groups was not statistically significant. The blood pressure reduction was not statistically significant possibly due to lack of statistical power. The number of subject was 12 in exercise training group. Thus, the fractionated exercise study used blood pressure as a primary outcome is warranted.

***POST EXERCISE HYPOTENSION***

Post exercise hypotension is a phenomenon of a sustained reduction in resting blood pressure following a single bout of exercise (63). Post exercise hypotension was first documented by L. Hill during the 90 min following a 400 yard dash (54). Only after Fitzgerald's anecdotal report of the effect of jogging on his own labile hypertension (28), the researchers began to thoroughly investigate this phenomenon. Post exercise hypotension is clinically significant because it provides health benefits associated with transiently lowered blood pressure (4). Further, post exercise hypotension might be attributed to blood pressure reduction with exercise training by accumulating hypotensive effects following each acute bout of exercise (125).

Post exercise hypotension occurs in response to several types of large muscle dynamic exercise such as walking, running, cycling, and swimming at submaximal intensities between 40% and 70% of peak aerobic capacity for 20 to 60 minutes (63). Post exercise hypotension is observed in both normotensive and hypertensive subjects but is generally greater in magnitude in hypertensive subjects (63, 75). Post exercise hypotension has been reported to persist for 2 to 4 hours under laboratory conditions in normotensive individuals (63). Post exercise hypotension is sustained for a prolonged period of time under free-living conditions up to 11 to 12 hours for systolic blood pressures (5-8 mm Hg) and/or up to 6 to 8 hours for diastolic blood pressure (6-8 mm Hg) (63, 77, 99, 138, 139) in hypertensive individuals. Post exercise hypotension appears to be unaffected

by gender, age (75) or exercise intensity (99). The mechanisms contributing to the post exercise hypotension is inconclusive yet.

**Potential Mechanisms of Post Exercise Hypotension**

Mean arterial pressure is a product of cardiac output and total peripheral resistance. The potential mechanisms of post exercise hypotension must result from the manipulation of cardiac output and/or total systemic vascular resistance. In this review, the reduction of cardiac output (41) as a mechanism for post exercise hypotension is not further discussed. The decrease in local and total systemic vascular resistances results in vasodilation (17, 46). The vasodilation is associated with sympathetic vascular regulation by a neural and a vascular components (45). The neural component of this vasodilation is a reduction in the outflow of sympathetic vasoconstrictor nerve activity to skeletal muscle vascular beds (sympathoinhibition). The vascular component refers to the attenuation of vascular response to sympathetic vasoconstriction, as well as the potential influence of local and circulating vasodilator substances. In this review of possible mechanisms of post exercise hypotension, the focus has made in this vasodilation on 1) sympathoinhibition and 2) vasodilator substances.

1) Sympathoinhibition

The influence of sympathetic nerve activity was studied during post exercise hypotension (30, 44-46, 63, 75). The muscle sympathetic nerve activity (MSNA) directly measures an indication of vascular tone. Plasma noradrenalin

concentration is used as an indirect measure of spill over from the sympathetic activity. Heart rate variability is also used as an indication of the autonomic nervous system control.

During post exercise hypotension, it has been shown that the sympathetic nerves that control vasoconstriction in the leg are inhibited (44). Muscle sympathetic nerve activity is controlled by the baroreceptor reflexes and cardiopulmonary receptor reflexes in a resting state. The baroreceptor reflex is reset to a higher set point and sympathetic activity is increased during exercise (84, 137). These reflexes are reset to lower pressures than pre-exercise pressures after exercise. Thus, sympathetic outflow from the central nervous system is low following exercise. Early studies in animals suggested that this sympathoinhibition might be the result of activation of endogenous opioid receptor pathways in the central nervous system (126). The central nervous system mechanisms involved in baroreceptor reflex resetting during exercise and post exercise hypotension are unknown.

2) Vasodilator Substances

In addition to reductions in sympathetic outflow, vascular responsiveness to adrenergic receptor stimulation is impaired during post exercise hypotension (44, 56). The mechanism of this impaired vascular responsiveness seen in post exercise hypotension is unknown. Impaired sympathetic outflow into vascular resistance could be the result of competition at the arterial smooth muscle such

as the release of local vasodilator substances or by modulation of the alpha adrenergic pathway either by presynaptic or postsynaptic inhibition (45).

Nitric oxide may be partly responsible for the impaired responsiveness to sympathetic outflow. Factors associated with dynamic exercise, such as cyclic wall stress induced by increased blood flow and catecholamines, stimulate the release of nitric oxide from the vascular endothelium. In healthy humans nitric oxide production may be increased after acute exercise (61). It is well established that nitric oxide attenuates the vasoconstrictor response to alpha adrenergic receptor stimulation. However, there are a number of other potential vasodilators such as prostaglandins, adenosine, potassium, increased CO2 and/or decreased O2 that could potentially modify alpha adrenergic responsiveness (45).

In conclusion, post exercise hypotension occurs in both normotensive and hypertensive subjects. Post exercise hypotension is clinically significant in hypertension due to its duration and magnitude of the transient reduction in blood pressure seen in free-living condition as well as in laboratory setting. For post exercise hypotension to be used as a lifestyle modification for the prevention of hypertension, the duration and magnitude of hypertension should be established for adults with prehypertension. The mechanisms of post exercise hypotension are studied although they are still inconclusive. Further investigation is warranted to investigate the mechanisms of post exercise hypotension in free-living condition.

### *POWER SPECTRAL ANALYSIS OF HEART RATE VARIABILITY*

A significant relationship between the autonomic nervous system and cardiovascular mortality has been documented (74). Heart rate variability is the analysis of variations of the intervals between consecutive normal heart beats. The clinical relevance of heart rate variability was first introduced when Hon and Lee observed that fetal distress was preceded by alternations in RR intervals before any significant heart rate change (55). In 1978, the association between the acute myocardial infarction mortality and reduced heart rate variability was first shown (144). An association between lethal arrhythmias and signs of either increased sympathetic or reduced vagal activity has been also reported (9). The heart rate variability became clinically important tool because it was found to be a strong and independent predictor of acute myocardial infarction mortality (9, 65, 128).

Although the variations in heart rate may be evaluated by time domain methods and frequency domain methods, frequency domain methods are further discussed in this review. Power spectral analysis of heart rate variability (heart rate variability) is a non-invasive measurement to assess the quantification of autonomic nervous system fluctuations in health and diseases including hypertension (1, 36, 81, 122). Heart rate variability is influenced by the interaction among spontaneous nervous input to the sinoatrial (SA) node, sympathetic and vagal efferent nerve activity, and humoral factors. The RR interval variations exist in resting conditions represent a fine tuning of the beat-to-beat control mechanisms. Vagal afferent stimulation leads to reflex excitation of

vagal efferent activity and inhibition of sympathetic efferent activity. The opposite reflex is controlled by the stimulation of sympathetic afferent activity. Efferent vagal activity also appears to be under tonic control by cardiac afferent sympathetic activity. Efferent sympathetic and vagal activities directed to the SA node are characterized by discharge with each cardiac cycle. Cardiac cycle can be modulated by central (e.g. vasomotor and respiratory centers) and peripheral (e.g. oscillation in arterial pressure and respiratory movements) oscillators. These oscillators generate rhythmic fluctuations in efferent neural discharge which manifest as short and long-term oscillation.

Although cardiac cycle is modulated by various systems, heart rate and rhythm are largely under the control of the autonomic nervous system. Parasympathetic activity is mediated by acetylcholine release, which has a very short latency period and high turnover rate. This relatively rapid response of acetylcholine enables the parasympathetic nervous system to regulate cardiac function on a beat to beat basis. Sympathetic activity is mediated by noradrenaline, which is reabsorbed and metabolized relatively slowly. Thus, changes in heart rate mediated by sympathetic activity are relatively slow. Because of these differences in neurotransmitter function the parasympathetic and sympathetic nervous systems tend to operate at different frequencies and variation in heart rate.

Spectral analysis is performed for both short-term (2 to 5 minutes) and long-term (24 hours). Spectral components are total power, high frequency (0.15-0.40 Hz) which reflects cardiac vagal activity, respiratory mechanical and

vagal-mediated influence (mainly vagal), low frequency (0.04-0.15 Hz), which reflects cardiac sympathetic and vagal activity as well as vascular sympathetic activity. Because of this dual modulation, measurement of low frequency component does not provide a direct quantitative index of sympathetic activity.

Thus, the term sympathetic modulation (106, 122), rather than sympathetic activity should be used in the analysis of heart rate variability. There are more variables such as the ratio of low frequency to high frequency, which is index of sympathovagal balance (22)as well as very low frequency (0.003-0.04 Hz), and ultra low frequency (<0.003 Hz) used in the study of heart rate variability (122). The physiological roles in very low and ultra low frequency components are not clear, but the decreases in the very low and ultra low frequency components were reported in post myocardiac mortality.

**Other Factors Affecting Heart Rate Variability**

Certain medications affect heart rate variability. Beta-adrenergic blockade prevents the rise in the low frequency component observed in the morning hours. Anti-arrhythmic drugs, low dose muscarinic receptor blockers, such as atropine and scopolamine (136), may produce a paradoxical increase in vagal efferent activity, as suggested by a decrease in heart rate (122). Little is known about the effects of the environment (e.g. type and nature of physical activity and of emotional circumstances) during long-term electrocardiogram recordings.

## Power Spectral Analysis of Heart Rate Variability in Hypertension and Exercise

Previous investigations using power spectral analysis of heart rate variability have led to findings of autonomic alterations in hypertensive individuals (27, 39, 92, 95, 96, 106, 122, 132). Increased sympathetic and reduced parasympathetic activity (27, 39) are among the characteristics of autonomic dysfunction found in hypertension. A progressive increase in low frequency power (indicating increased sympathetic activity) and a decrease in high frequency (indicating decreased parasympathetic activity) power of heart rate variability with increasing severity of hypertension have been also reported (92). Moreover, augmented heart rate variability is associated with new onset of hypertension (116). Augmented sympathetic activity in normotensive individuals with a family history of hypertension (20) as compared to normotensive individuals with no family history was has been reported.

Exercise training is well known for its ability to restore impaired autonomic nervous system (6, 34, 36, 122). In epidemiology study moderate and vigorous physical activity was also associated with higher heart rate variability (109). In cross-sectional studies using power spectral analysis of heart rate variability investigators found an enhanced vagal tone in athletes (8, 79). Exercise training induced to restore autonomic nervous function measured by power spectral analysis of heart rate variability in various populations including hypertensive (49, 57, 58, 80, 83, 93, 114, 115, 123, 129, 131). These exercise training studies are summarized in Table 3.

Table 3. Summary of selected studies investigation HRV in exercise training

| Author of Study | Population | Types of Exercise | Investigation parameter | Clinical Findings |
|---|---|---|---|---|
| Hautala (49) | 20 healthy | 70-80% of HRmax | Long-term (24-hour) | ↑ HF |
| Howarka (57) | 8 diabetics | 65% of maximal performance | Short-term (5 min) | ↑ LF<br>↑ HF<br>↑ Total |
| Iwasaki (58) | 11 sedentary | Progressive training | Short-term (6 min) | ↑ LF |
| Malfatto (80) | 22 post myocardial infarction | Cardiac Endurance training | Short-term (5 min) | ↓ LF:HF |
| Melanson (83) | 11 sedentary men | 80% of $VO_2$max | Short-term (5 min) | ↑ HF |
| Pagani (93) | 11 hypertensive | 20 min jogging | Short-term (20 min) | ↑ HF<br>↓ LF |
| Schuit (114) | 27 elderly | 70-80% of HRmax | Long-term (24-hour) | ↑ LF |
| Seals (115) | 11 healthy | 70-80% of HRR | Short-term (5 min) | ↑ Total |
| Taylor (123) | 9 hypertensive | 30% of MVC | Short-term (10 min) | ↑ HF |
| Tulppo (129) | 20 sedentary | 70-80% of HRmax | Long-term (24-hour) | ↑ HF<br>↓ LF |
| Uusitalo (131) | 47 elderly | 40-60% of $VO_2$max | Short-term (5 min) | ↓ LF |

HRmax: maximum heart rate; $VO_2$max: maximal oxygen consumption; HRR: heart rate reserve; LF: low frequency power of heart rate variability; HF: high frequency power of heart rate variability; LF:HF; the ratio of low to high frequency power; Total: total power of heart rate variability; ↑: increase; ↓: decrease

Reduced sympathetic activity is one of the possible mechanisms of post exercise hypotension (12, 18, 30, 45, 66, 75). There are only a few studies using short-term power spectral analysis of heart rate variability to assess autonomic function during post exercise hypotension (69, 76) under laboratory condition. MacDonald et al. showed increased parasympathetic activity during subsequent bouts of exercise after acute exercise (70% of $VO_2$peak for 30 minutes) using short-term heart rate variability (76). Legramante et al., however, failed to see the changes in sympathetic modulation 60 to 90 minutes following maximal exercise test (69). Studies using long-term heart rate variability, however, would be of interest in post exercise hypotension studies because post exercise hypotension persists up to 11 to 12 hours under free-living conditions (63, 77, 99, 138, 139). Furthermore, changes in cardiac autonomic regulation was found several hours after cessation of acute exercise measured by heart rate variability (48, 102).

In summary, power spectral analysis of heart rate variability has been commonly used to quantify the relative dominance of vagal and sympathetic influence on the heart. Exercise induces the restoration of autonomic regulation. There are limited studies using power spectral analysis of heart rate variability to investigate autonomic regulation during post exercise hypotension.

### *AMBULATORY BLOOD PRESSURE MONITORING*

While auscultation of the Korotkoff sounds remains the established standard technique for blood pressure measurement in clinical medicine (119),

ambulatory blood pressure monitoring is widely used in both clinical and research settings in order to achieve more information about an individual's blood pressure during activities of daily living. Diurnal blood pressure profiles exhibit higher values when individuals are awake and mentally and physically active, and lower values when sleeping and resting (15). Ambulatory blood pressure values are typically lower than those obtained in a clinical office (15, 24, 145), with a 24-hour average ambulatory blood pressure of 125/80 mm Hg corresponding to an office value of 140/90 mm Hg (24, 145). Ambulatory blood pressure monitoring should not be regarded as a substitute for office blood pressure measurement (15, 16, 24, 145) due to limited data available regarding prognostic value.

There are many advantages of ambulatory blood pressure monitoring. Measuring blood pressure in a clinical setting is confounded by the occurrence of "white-coat hypertension" (15, 24, 145), the elevated clinic blood pressure in the presence of normal ambulatory blood pressure. "White-coat hypertension" occurs in as many as 20 to 35% of hypertensive patients (101). Ambulatory blood pressure monitoring can differentiate between white-coat hypertension and actual hypertension (15, 24, 143, 145). Ambulatory blood pressure monitoring also correlates with hypertensive target organ damage more closely than does office blood pressure (15, 24, 82, 145), and predicts additional risk of cardiovascular events after adjustment for office blood pressure (15, 24, 118, 145). In addition, ambulatory blood pressure monitoring has been used as a research tool. For example, the duration and magnitude of post exercise hypotension have been identified in free-living condition (31, 98, 100, 139).

There are a number of factors to affect ambulatory blood pressure measurements such as the monitors themselves. Standard protocols exist for evaluating the accuracy of blood pressure measurements (Association for the Advancement of Medical Instrumentation (AAMI), 1987; British Hypertension Society (BHS), 1990; European Society of Hypertension, 2002) (89). These protocols had a common objective to establish the standards of accuracy and performance and to facilitate the comparison of one device with another. To meet AAMI criteria, the mean difference between the device and the mercury standard must be <5 mm Hg or the standard deviation must be <8 mm Hg. To meet BHS criteria, devices must achieve a grade of at least a 'B' for both systolic and diastolic measurements. A grade of 'A' denotes greatest agreement and 'D' denotes least agreement with the mercury standard. Ambulatory blood pressure monitoring devices have been validated for use in specific groups and in different circumstances based on these protocols.

The Accutracker II (SunTech Medical Instruments, Morrisville, NC) has been validated using the standard protocols by AAMI and BHS (4, 89, 124), with the mean differences by the Accutracker II and the observers -2.2+0.8/-3.5+0.9 mm Hg (124). Inter-device variability of the Accutracker II was small but significant although all the devices met the BHS criteria. The day to day reproducibility of the Accutracker II has been examined in control conditions (70). Intraclass correlation coefficients for daytime (6:00a.m. to 10:00p.m.) and nighttime (10:00p.m. to 6:00a.m.) averages were 0.95, 0.96, and 0.86 for systolic blood pressure, and 0.90, 0.90, and 0.83 for diastolic blood pressure,

respectively. The Accutracker II fulfilled the AAMI criteria although it was graded A for systolic and C for diastolic blood pressure using the BHS system (90, 124).

The reproducibility of ambulatory blood pressure measurements has been reported to be higher than clinic measurements (60, 105, 127). The reproducibility of ambulatory blood pressure measurements has been performed on two to four separate days of 24-hour measurements (52, 88) or on one to two days of 48-hour measurement (51, 105). The ranges of the correlation coefficients between two 24-hour ambulatory blood pressure measurements are 0.81 to 0.91 depending on the ambulatory variable measured (52). Systolic ambulatory blood pressure measurement is more reliable than diastolic ambulatory blood pressure measurement (108). Day-to-day differences in average 24-hour blood pressure have also been reported (94) likely a result of biological variability, daily activity, or stress, however. Further, a significant elevation in systolic and diastolic pressures has been reported for the first two to eight hours of one 48 hour monitoring session (51, 105).

There are other factors affecting ambulatory blood pressure monitoring. Ambulatory blood pressure monitoring can produce artifacts due to inappropriate cuff size and interference with sleep (119). There is a transient increase in systolic blood pressure averaging 5 to 15 mm Hg due to these artifacts (119). Strategies for optimizing ambulatory blood pressure monitoring include appropriate subject selection and instruction as well as editing criteria (94). Because the time of day to begin the ambulatory monitoring influences the

outcome, the time of day to begin the monitoring should be considered an additional factor to be controlled (140).

In summary, ambulatory blood pressure monitoring is widely used in both clinical and research settings in order to observe blood pressure during activities of daily living. The validity of each ambulatory blood pressure monitor needs to be evaluated by standard protocols for an accurate outcome. Ambulatory blood pressure measurements are more reliable than are clinic measurements. Other factors such as appropriate cuff and time of day to begin monitor have been identified to improve the reliability of ambulatory blood pressure measurements.

### *PHYSICAL ACTIVITY MONITORING*

Accelerometers directly and objectively measure and quantify physical activity throughout the day. Accelerometers, which convert measured kinetic energy into electrical energy and translate it into acceleration data, are more often used in research because they provide more information about physical activity, such as the intensity, frequency and duration. Accelerometers are also more sensitive to low-intensity activities (50, 68, 121). This greater sensitivity comes at a price, however, as it can be a source of artifact, with background vibration (e.g., when moving in a vehicle) being recorded as movement (68).

A triaxial accelerometer is based on three orthogonally mounted uniaxial (vertical, anterioposterior, mediolateral axes) accelerometers. Bouten et al. (1994) (11) reported that the sum of the integrals from all three axes was most strongly correlated to an activity energy expenditure measured by indirect

calorimetry (r=0.95) rather than three individual axes. The units of accelerometers (activity count or vector magnitude), however, are not standardized. Furthermore, several accelerometers provide energy expenditure from different regression equations, which contributes to their source of error. Freedson and Miller have recommended using movement counts rather than energy expenditure, which is computed from a regression equation and is therefore a possible source of error (33).

The RT3 is a newer version of the Tritrac from the same company. The RT3 is a small (68 X 48 X18 mm), lightweight (65.2 g), battery-powered triaxial accelerometer, with three orthogonal axes (vertical, X; anterioposterior, Y; and mediolateral, Z). The four operation options of RT3 are following: 1) mode 1 and 3 sample and store activity counts on individual axes but use different epoch durations, 1-s epoch for mode 1- and 60-s epoch for mode 3, 2) mode 2 and 4 sample and store vector magnitude ($V_m = [X^2 + Y^2 + Z^2]^{0.5}$) activity counts but use different epoch durations, 1-s epoch for mode 1 and 60-s epoch for mode 3. In RT3, the conversion of acceleration counts to caloric expenditure is calculated using exactly the same equations as the Tritrac. In contrast to the Tritrac, the RT3 uses an integrated triaxial accelerometer that integrates measurement of the three vectors into a single chip.

The validity and reliability of the RT3 have been investigated only in a few studies. The Tritrac, the previous version of RT3, has been successfully correlated against oxygen uptake in the laboratory (r=0.86) (11) and in the field (r=0.62) (23). The intraclass correlation of inter-instruments, RT3 accelerometers

for activity accounts is 0.99 regardless of axes (103). Rowlands et al. (111) recently validated RT3 for the assessment of physical activity. The physical activity using RT3 was significantly correlated to oxygen uptake in boys (r=0.87) and in men (r=0.85). Vector magnitude was superior to estimate energy expenditure in boys but not in men. The vector magnitude is a composite three-dimensional signal. RT3 counts were significantly higher than Tritrac counts. This difference is largely due to the anteroposterior vector, which has high variability. Powell and Rowlands (104) reported that inter-monitor variability of RT3 was <6% during locomotion. Inter-monitor variability at each activity increased as intensity increased. The validity of RT3 to predict oxygen consumption is as good as Tritrac, although the activity counts from the two monitors are not comparable. When assessing locomotion, body size adds significantly to the variance explained in oxygen consumption by activity counts (111).

In conclusion, the RT3 has been reported reliable. Intermonitor variability exists, however. The vertical axis of the RT3 accelerometer showed the least variability and was the most reliable.

***SUMMARY***

Hypertension has long been known to be a major modifiable risk factor for cardiovascular diseases stroke (78), coronary artery disease (78), congestive heart failure (135), and end-stage renal disease (64). Aerobic exercise is well established as a lifestyle modification for treatment of hypertension. Several

health organizations, including the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (14), the American Heart Association (29), and the American College of Sports Medicine (3), have published policy statements recommending the daily accumulation of physical activity to prevent and/or to treat hypertension. There is lack of evidence supporting the daily accumulation of physical activity as a new exercise prescription for the prevention of hypertension

A sustained reduction in resting blood pressure following a single bout of aerobic exercise has been defined as post exercise hypotension. The mechanisms of post exercise hypotension are not fully understood, yet. Sympathetic modulation is one of the possible mechanisms of post exercise hypotension (45, 75). Excess sympathetic activity is also found in heart failure and myocardial infarction (9, 65, 144). Thus, the investigation of sympathetic modulation as a possible mechanism of post exercise hypotension has merit of clinical utility. No study exists to explore the sympathetic mechanisms of post exercise hypotension during the activities of daily living.

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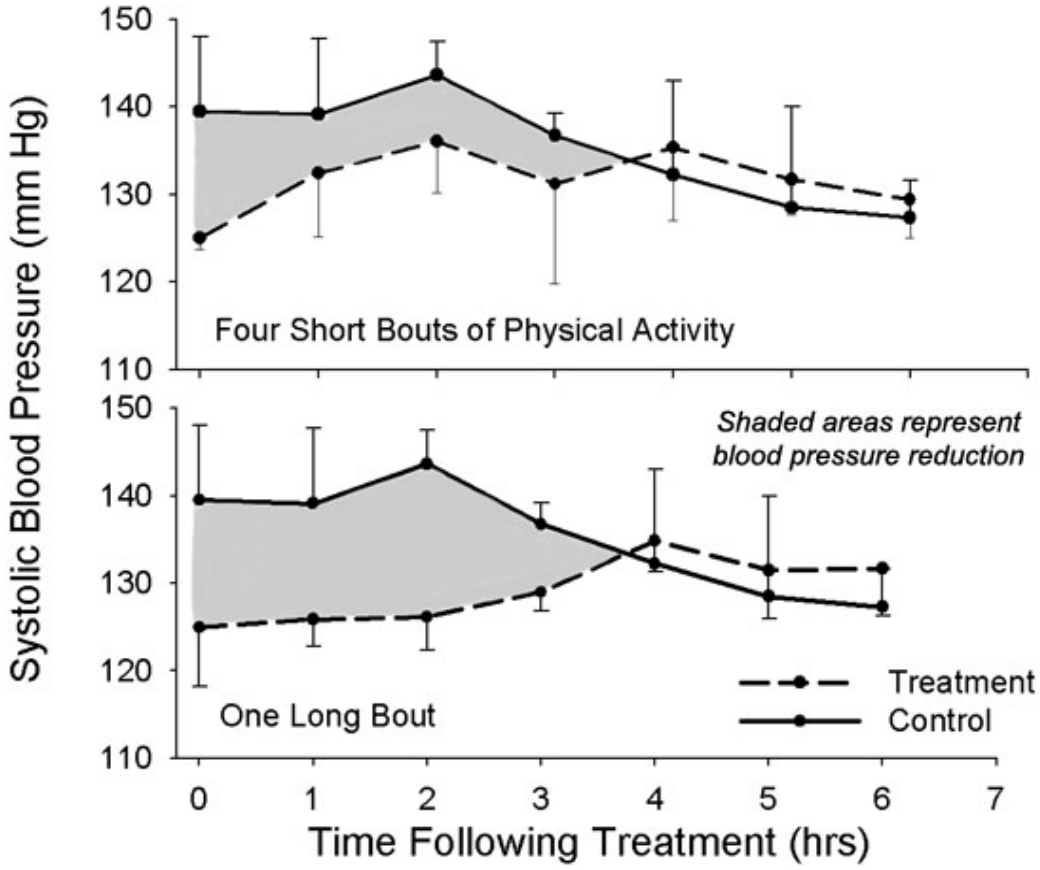
## *APPENDIX B - PILOT STUDY*

The accumulation of physical activity rather than one continuous physical activity has been recommended for the treatment of hypertension and prehypertension although the efficacy of the accumulation of physical activity is not well established for the treatment of prehypertension. The purpose of the pilot study was 1) to compare the duration and magnitude of blood pressure reduction following the accumulation of physical activity and one continuous physical activity, and 2) to observe sympathetic modulation as a possible mechanism for blood pressure reduction in prehypertension.

Pilot data was collected on two adults with prehypertension. One was a 55 years old woman who had a systolic blood pressure of 127 mm Hg and a diastolic blood pressure of 78 mm Hg. The other subject was a 34 years old man who had a systolic blood pressure of 133 mm Hg and a diastolic blood pressure of 82 mm Hg. Blood pressure using ambulatory blood pressure monitoring and sympathetic modulation using Holter monitoring were measured for 12 hours following one continuous physical activity (40 min), following the accumulation of four short (10 min) sessions of physical activity and following a control. The intensity of both physical activity treatments was same. All activity was performed on a motor driven treadmill.

These data are illustrated in Figure 2. The duration of blood pressure reduction following the two treatments appears the same (accumulation =3 hr; long=3 hr), but the magnitude may be greater following one long bout than following the accumulation of four short bouts.

***FIGURE 1.*** Ambulatory systolic blood pressure response (mean±SE) of two adults with prehypertension following the accumulation of four short bouts of physical activity and one long bout of physical activity.




Sympathetic modulation was summarized in Table 1. Normalized high frequency power (parasympathetic activity) showed a progressive increase from control to the accumulation of four short bouts of physical activity and to the single long bout of physical activity. Normalized low frequency power and the ratio of low to high frequency power exhibited decreases following both treatments.

***TABLE 1.*** Sympathetic modulation by heart rate variability following the accumulation of four short bouts of physical activity (Short) and one long bout of (Long) physical activity treatments

| ***Normalized Low Frequency Power (%)*** | | | ***Normalized High Frequency Power (%)*** | | | ***Ratio of Low to High Frequency Power*** | | |
|---|---|---|---|---|---|---|---|---|
| **Control** | **Short** | **Long** | **Control** | **Short** | **Long** | **Control** | **Short** | **Long** |
| 89.9 | 71.5 | 81.7 | 9.1 | 18.2 | 16.56 | 9.89 | 3.92 | 4.94 |

These data are promising. Blood pressure reductions were detected in both the accumulation of short bouts of physical activity as well as one long bout of physical activity treatments. Hence, the efficacy of physical activity as a treatment for hypertension can be investigated in this paradigm.

## *APPENDIX C - RAW DATA TABLES*

***TABLE 1. DEMOGRAPHICS OF SUBJECTS***

| ID | Sex | Age (yrs) | Height (cm) | Weight (kg) | BMI ($kg \cdot m^{-2}$) | $VO_2$peak ($ml \cdot kg^{-1} \cdot min^{-1}$) |
|---|---|---|---|---|---|---|
| R2000 | M | 25 | 177.9 | 85.7 | 44.1 | 26.4 |
| R2001 | M | 35 | 178.5 | 111.2 | 50.4 | 30.2 |
| R2002 | M | 32 | 177.6 | 90.9 | 49.4 | 37.2 |
| R2003 | M | 51 | 178.0 | 88.1 | 47.1 | 29.7 |
| R2004 | F | 64 | 156.0 | 46.4 | 40.7 | 28.1 |
| R2005 | M | 28 | 177.1 | 113.7 | 39.6 | 34.8 |
| R2006 | M | 55 | 185.0 | 78.9 | 53.3 | 34.6 |
| R2007 | F | 58 | 175.0 | 66.0 | 49.6 | 29.4 |
| R2008 | F | 62 | 170.1 | 71.7 | 40.9 | 25.8 |
| R2009 | M | 47 | 181.0 | 74.4 | 45.2 | 48.7 |
| R2010 | M | 36 | 175.8 | 81.1 | 49.7 | 41.2 |
| R2011 | M | 66 | 180.0 | 82.0 | 56.8 | 34.6 |
| R2012 | F | 66 | 178.0 | 73.0 | 50.9 | 24.9 |
| R2013 | M | 46 | 163.0 | 81.0 | 44.2 | 43.9 |
| R2014 | M | 50 | 180.2 | 91.6 | 54.7 | 39.4 |
| R2015 | F | 61 | 165.0 | 63.4 | 44.4 | 26.6 |
| R2017 | M | 45 | 181.3 | 88.4 | 50.8 | 46.0 |
| R2018 | M | 40 | 184.8 | 138.1 | 46.3 | 29.0 |
| R2019 | M | 43 | 186.7 | 86.2 | 47.2 | 43.6 |
| R2020 | M | 33 | 175.3 | 77.7 | 46.2 | 35.6 |
| Mean | | 47.2 | 176.32 | 84.47 | 27.00 | 34.48 |
| SD | | 13.06 | 7.63 | 19.61 | 5.23 | 7.31 |
| SE | | 2.92 | 1.71 | 4.39 | 1.17 | 1.64 |

BMI = body mass index, $VO_2$peak = peak oxygen uptake

***TABLE 2. SCREENING BLOOD PRESSURE***

| ID | SBP (mm Hg) | DBP (mm Hg) |
|---|---|---|
| R2000 | 138 | 84 |
| R2001 | 130 | 85 |
| R2002 | 132 | 86 |
| R2003 | 132 | 82 |
| R2004 | 130 | 69 |
| R2005 | 137 | 74 |
| R2006 | 123 | 81 |
| R2007 | 134 | 89 |
| R2008 | 130 | 70 |
| R2009 | 140 | 88 |
| R2010 | 129 | 82 |
| R2011 | 125 | 88 |
| R2012 | 131 | 87 |
| R2013 | 130 | 74 |
| R2014 | 127 | 88 |
| R2015 | 134 | 80 |
| R2017 | 126 | 81 |
| R2018 | 137 | 87 |
| R2019 | 135 | 86 |
| R2020 | 138 | 88 |
| Mean | 131.8 | 82.5 |
| SD | 4.72 | 7.29 |
| SE | 1.05 | 1.63 |

SBP = systolic blood pressure, DBP = diastolic blood pressure

Blood pressure was averaged based upon a total of six measurements.

***TABLE 3. ORDER OF TREATMENTS AND NUMBER OF DAYS BETWEEN PHYSICAL ACTIVITY TREATMENTS***

| ID | Order of treatments | # of days between PA treatments |
|---|---|---|
| R2000 | 1-3-2 | 7 |
| R2001 | 2-1-3 | 7 |
| R2002 | 1-3-2 | 28 |
| R2003 | 2-1-3 | 10 |
| R2004 | 3-1-2 | 21 |
| R2005 | 3-2-1 | 8 |
| R2006 | 1-2-3 | 27 |
| R2007 | 3-1-2 | 7 |
| R2008 | 2-3-1 | 7 |
| R2009 | 2-1-3 | 21 |
| R2010 | 1-3-2 | 28 |
| R2011 | 3-1-2 | 41 |
| R2012 | 1-3-2 | 23 |
| R2013 | 3-1-2 | 7 |
| R2014 | 3-1-2 | 16 |
| R2015 | 2-1-3 | 35 |
| R2017 | 1-2-3 | 11 |
| R2018 | 1-3-2 | 7 |
| R2019 | 3-1-2 | 8 |
| R2020 | 3-2-1 | 14 |
| Mean | | 16.7 |
| SD | | 10.40 |
| SE | | 2.33 |

PA = physical activity

1 = control treatment, 2 = the accumulation of physical activity treatment, 3 = a continuous physical activity treatment

***TABLE 4. CARDIORESPIRATORY DATA***

| ID | $VO_2$peak ($ml \cdot kg^{-1} \cdot min^{-1}$) | max HR (bpm) | 50% $VO_2$peak ($ml \cdot kg^{-1} \cdot min^{-1}$) | $VO_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$) | $VO_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$) | PA Intensity (%) | |
|---|---|---|---|---|---|---|---|
| | | | Target | Short Ex | Long Ex | Short Ex | Long Ex |
| R2000 | 26.4 | 199 | 13.20 | 13.2 | 13.6 | 13.2 | 51.4 |
| R2001 | 30.2 | 188 | 14.92 | 14.9 | 15.5 | 15.5 | 51.9 |
| R2002 | 37.2 | 191 | 18.59 | 18.6 | 20.5 | 19.5 | 55.0 |
| R2003 | 29.7 | 181 | 14.83 | 14.8 | 15.5 | 15.0 | 52.1 |
| R2004 | 28.1 | 179 | 14.05 | 14.1 | 14.5 | 14.2 | 51.6 |
| R2005 | 34.8 | 200 | 17.41 | 17.4 | 17.5 | 17.5 | 50.3 |
| R2006 | 34.6 | 179 | 17.30 | 17.3 | 17.4 | 17.2 | 50.3 |
| R2007 | 29.4 | 189 | 14.70 | 14.7 | 15.1 | 16.3 | 51.2 |
| R2008 | 25.8 | 166 | 12.90 | 12.9 | 13.2 | 13.4 | 51.1 |
| R2009 | 48.7 | 188 | 24.35 | 24.4 | 26.2 | 24.0 | 53.8 |
| R2010 | 41.2 | 186 | 20.60 | 20.6 | 20.5 | 20.8 | 49.6 |
| R2011 | 34.6 | 178 | 17.29 | 17.3 | 16.6 | 17.0 | 48.0 |
| R2012 | 24.9 | 175 | 12.43 | 12.4 | 13.8 | 12.7 | 55.7 |
| R2013 | 43.9 | 188 | 21.96 | 22.0 | 21.3 | 22.5 | 48.6 |
| R2014 | 39.4 | 197 | 19.68 | 19.7 | 20.0 | 20.8 | 50.8 |
| R2015 | 26.6 | 176 | 13.31 | 13.3 | 14.9 | 16.6 | 55.9 |
| R2017 | 46.0 | 190 | 23.00 | 23.0 | 22.6 | 23.5 | 49.2 |
| R2018 | 29.0 | 172 | 14.52 | 14.5 | 15.1 | 14.7 | 52.1 |
| R2019 | 43.6 | 199 | 21.78 | 21.8 | 25.2 | 23.1 | 57.9 |
| R2020 | 35.6 | 190 | 17.80 | 17.8 | 18.3 | 18.0 | 51.3 |
| Mean | 34.46 | 185.6 | 17.23 | 17.86 | 17.78 | 51.89 | 51.74 |
| SD | 7.14 | 9.31 | 3.57 | 3.76 | 3.54 | 2.52 | 2.84 |
| SE | 1.60 | 2.08 | 0.80 | 0.84 | 0.79 | 0.56 | 0.63 |

$VO_2$peak = peak oxygen uptake, HR = heart rate, PA = physical activity, $VO_2$ = oxygen uptake

***TABLE 5. AMBULATORY BLOOD PRESSURE MONITORING FOR 12-HOUR MEASUREMENTS***

| | | *CONTROL* | | |
|---|---|---|---|---|
| **ID** | **Starting Time** | **Sampled** | **Used** | **%** |
| R2000 | 12:58 | 68 | 59 | 86.8 |
| R2001 | 12:56 | 53 | 50 | 94.3 |
| R2002 | 12:51 | 53 | 49 | 92.5 |
| R2003 | 12:40 | 53 | 51 | 96.2 |
| R2004 | 13:00 | 55 | 54 | 98.2 |
| R2005 | 13:00 | 54 | 46 | 85.2 |
| R2006 | 12:20 | 50 | 49 | 98.0 |
| R2007 | 11:50 | 64 | 60 | 93.8 |
| R2008 | 12:16 | 51 | 48 | 94.1 |
| R2009 | 12:24 | 50 | 49 | 98.0 |
| R2010 | 12:32 | 66 | 58 | 87.9 |
| R2011 | 12:29 | 64 | 45 | 70.3 |
| R2012 | 12:42 | 50 | 50 | 100.0 |
| R2013 | 12:53 | 53 | 53 | 100.0 |
| R2014 | 12:53 | 54 | 50 | 92.6 |
| R2015 | 12:23 | 54 | 54 | 100.0 |
| R2017 | 12:59 | 51 | 50 | 98.0 |
| R2018 | 12:25 | 54 | 53 | 98.1 |
| R2019 | 12:53 | 56 | 53 | 94.6 |
| R2020 | 13:39 | 51 | 50 | 98.0 |
| Mean | 12:42:09 | 55.2 | 51.6 | 93.83 |
| SD | 0:23 | 5.60 | 4.01 | 7.05 |
| SE | 0:05 | 1.25 | 0.90 | 1.58 |

***TABLE 5. (CONTINUED) AMBULATORY BLOOD PRESSURE MONITORING FOR 12-HOUR MEASUREMENTS***

| | | ***ACCUMULATION*** | | |
|---|---|---|---|---|
| **ID** | **Starting Time** | **Sampled** | **Used** | **%** |
| R2000 | 12:50 | 51 | 46 | 90.2 |
| R2001 | 13:18 | 53 | 49 | 92.5 |
| R2002 | 12:57 | 48 | 47 | 97.9 |
| R2003 | 12:46 | 59 | 35 | 59.3 |
| R2004 | 13:04 | 53 | 49 | 92.5 |
| R2005 | 13:03 | 52 | 44 | 84.6 |
| R2006 | 12:01 | 53 | 51 | 96.2 |
| R2007 | 12:26 | 60 | 60 | 100.0 |
| R2008 | 12:18 | 55 | 52 | 94.5 |
| R2009 | 12:24 | 56 | 56 | 100.0 |
| R2010 | 12:31 | 53 | 50 | 94.3 |
| R2011 | 12:44 | 64 | 44 | 68.8 |
| R2012 | 13:04 | 49 | 49 | 100.0 |
| R2013 | 12:59 | 50 | 49 | 98.0 |
| R2014 | 12:53 | 37 | 36 | 97.3 |
| R2015 | 12:22 | 53 | 53 | 100.0 |
| R2017 | 13:04 | 54 | 50 | 92.6 |
| R2018 | 12:40 | 51 | 47 | 92.2 |
| R2019 | 12:58 | 52 | 49 | 94.2 |
| R2020 | 13:47 | 47 | 45 | 95.7 |
| Mean | 12:48:27 | 52.5 | 48.1 | 92.04 |
| SD | 0:23 | 5.46 | 5.76 | 10.44 |
| SE | 0:05 | 1.22 | 1.29 | 2.33 |

***TABLE 5. (CONTINUED) AMBULATORY BLOOD PRESSURE MONITORING FOR 12-HOUR MEASUREMENTS***

| | | ***CONTINUOUS*** | | |
|---|---|---|---|---|
| **ID** | **Starting Time** | **Sampled** | **Used** | **%** |
| R2000 | 13:09 | 52 | 47 | 90.4 |
| R2001 | 12:48 | 57 | 49 | 86.0 |
| R2002 | 12:47 | 53 | 50 | 94.3 |
| R2003 | 12:47 | 52 | 46 | 88.5 |
| R2004 | 13:00 | 55 | 51 | 92.7 |
| R2005 | 13:07 | 58 | 50 | 86.2 |
| R2006 | 12:26 | 51 | 50 | 98.0 |
| R2007 | 12:39 | 51 | 49 | 96.1 |
| R2008 | 12:19 | 54 | 54 | 100.0 |
| R2009 | 13:01 | 51 | 43 | 84.3 |
| R2010 | 12:51 | 58 | 55 | 94.8 |
| R2011 | 13:02 | 68 | 44 | 64.7 |
| R2012 | 12:47 | 46 | 46 | 100.0 |
| R2013 | 13:20 | 50 | 48 | 96.0 |
| R2014 | 13:03 | 54 | 47 | 87.0 |
| R2015 | 12:32 | 57 | 54 | 94.7 |
| R2017 | 13:35 | 46 | 43 | 93.5 |
| R2018 | 12:43 | 55 | 48 | 87.3 |
| R2019 | 13:08 | 49 | 48 | 98.0 |
| R2020 | 13:51 | 51 | 51 | 100.0 |
| Mean | 12:56:45 | 53.4 | 48.7 | 91.63 |
| SD | 0:22 | 4.89 | 3.41 | 8.12 |
| SE | 0:04 | 1.09 | 0.76 | 1.82 |

***TABLE 6A. HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING A CONTROL TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 143 | 143 | 159 | 141 | 136 | 122 | 134 | 145 |
| R2001 | 130 | 144 | 140 | 132 | 139 | 133 | 133 | 126 |
| R2002 | 139 | 139 | 135 | 135 | 134 | 134 | 139 | 129 |
| R2003 | 122 | 137 | 120 | 126 | 132 | 134 | 134 | 128 |
| R2004 | 122 | 117 | 98 | 111 | 108 | 109 | 115 | 107 |
| R2005 | 166 | 162 | 172 | 153 | 160 | 131 | 128 | 134 |
| R2006 | 122 | 126 | 134 | 134 | 121 | 129 | 119 | 109 |
| R2007 | 139 | 131 | 130 | 130 | 129 | 128 | 120 | 134 |
| R2008 | 117 | 132 | 129 | 144 | 127 | 132 | 118 | 119 |
| R2009 | 140 | 141 | 140 | 150 | 153 | 151 | 158 | 140 |
| R2010 | 136 | 134 | 137 | 130 | 130 | 148 | 135 | 127 |
| R2011 | 133 | 136 | 125 | 139 | 126 | 129 | 133 | 127 |
| R2012 | 138 | 147 | 158 | 149 | 141 | 146 | 134 | 140 |
| R2013 | 130 | 131 | 147 | 131 | 133 | 126 | 130 | 136 |
| R2014 | 136 | 149 | 119 | 118 | 119 | 129 | 146 | 153 |
| R2015 | 136 | 151 | 139 | 130 | 146 | 136 | 136 | 125 |
| R2017 | 140 | 140 | 133 | 131 | 136 | 140 | 141 | 146 |
| R2018 | 129 | 129 | 124 | 123 | 134 | 139 | 137 | 134 |
| R2019 | 133 | 119 | 130 | 130 | 112 | 128 | 122 | 129 |
| R2020 | 152 | 136 | 139 | 135 | 138 | 131 | 142 | 142 |
| Mean | 135.0 | 137.2 | 135.3 | 133.6 | 132.6 | 132.7 | 132.6 | 131.3 |
| SD | 11.16 | 10.82 | 15.97 | 10.38 | 12.52 | 9.43 | 10.48 | 11.49 |
| SE | 2.49 | 2.42 | 3.57 | 2.32 | 2.80 | 2.11 | 2.34 | 2.57 |

***TABLE 6A. (CONTINUED) HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING A CONTROL TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 163 | 151 | 149 | 112 |
| R2001 | 128 | 129 | 113 | 110 |
| R2002 | 132 | 120 | 117 | 109 |
| R2003 | 127 | 124 | 124 | 120 |
| R2004 | 120 | 112 | 102 | 102 |
| R2005 | 113 | 112 | 82 | 93 |
| R2006 | 118 | 127 | 122 | 118 |
| R2007 | | | | |
| R2008 | 111 | 102 | 113 | 109 |
| R2009 | 150 | 153 | 156 | 137 |
| R2010 | 127 | 123 | 130 | 123 |
| R2011 | 136 | 113 | 108 | 111 |
| R2012 | 130 | 132 | 106 | 95 |
| R2013 | 149 | 127 | 132 | 118 |
| R2014 | 139 | 145 | 149 | 145 |
| R2015 | 128 | 143 | 141 | 114 |
| R2017 | 140 | 135 | 139 | 119 |
| R2018 | 140 | 139 | 140 | 110 |
| R2019 | 128 | 125 | 107 | 111 |
| R2020 | 142 | 128 | 122 | 121 |
| Mean | 132.7 | 128.3 | 123.8 | 114.5 |
| SD | 13.14 | 13.78 | 19.19 | 12.31 |
| SE | 2.94 | 3.08 | 4.29 | 2.75 |

***TABLE 6B. HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING A CONTROL TREATMENT***

| | Hourly mean blood pressure (mm Hg) following a treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 93 | 93 | 99 | 99 | 102 | 99 | 101 | 92 |
| R2001 | 91 | 94 | 94 | 80 | 79 | 72 | 85 | 71 |
| R2002 | 91 | 96 | 87 | 88 | 90 | 91 | 85 | 88 |
| R2003 | 87 | 73 | 83 | 87 | 93 | 87 | 90 | 84 |
| R2004 | 61 | 70 | 58 | 61 | 61 | 62 | 68 | 62 |
| R2005 | 81 | 82 | 90 | 79 | 88 | 76 | 79 | 75 |
| R2006 | 69 | 66 | 70 | 76 | 77 | 70 | 70 | 69 |
| R2007 | 91 | 90 | 88 | 83 | 82 | 87 | 85 | 92 |
| R2008 | 76 | 74 | 70 | 74 | 68 | 70 | 68 | 70 |
| R2009 | 86 | 89 | 90 | 94 | 99 | 99 | 101 | 89 |
| R2010 | 87 | 89 | 88 | 86 | 87 | 82 | 78 | 80 |
| R2011 | 86 | 82 | 86 | 86 | 94 | 100 | 89 | 80 |
| R2012 | 83 | 83 | 85 | 86 | 88 | 86 | 85 | 87 |
| R2013 | 87 | 79 | 82 | 83 | 80 | 85 | 84 | 87 |
| R2014 | 90 | 80 | 75 | 75 | 76 | 85 | 88 | 86 |
| R2015 | 75 | 82 | 80 | 74 | 77 | 73 | 77 | 71 |
| R2017 | 79 | 80 | 81 | 80 | 86 | 87 | 82 | 81 |
| R2018 | 71 | 75 | 75 | 71 | 78 | 77 | 77 | 81 |
| R2019 | 77 | 72 | 82 | 71 | 69 | 67 | 75 | 73 |
| R2020 | 86 | 82 | 77 | 84 | 78 | 77 | 93 | 88 |
| Mean | 82.3 | 81.5 | 81.8 | 80.6 | 82.5 | 81.5 | 83.0 | 80.2 |
| SD | 8.55 | 8.43 | 9.40 | 8.78 | 10.35 | 11.00 | 9.39 | 8.62 |
| SE | 1.91 | 1.88 | 2.10 | 1.96 | 2.31 | 2.46 | 2.10 | 1.93 |

***TABLE 6B. (CONTINUED) HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING A CONTROL TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 103 | 100 | 73 | 72 |
| R2001 | 75 | 68 | 61 | 62 |
| R2002 | 84 | 78 | 78 | 74 |
| R2003 | 86 | 77 | 78 | 77 |
| R2004 | 69 | 63 | 64 | 59 |
| R2005 | 59 | 58 | 42 | 48 |
| R2006 | 76 | 74 | 72 | 70 |
| R2007 | | | | |
| R2008 | 63 | 63 | 67 | 64 |
| R2009 | 96 | 99 | 97 | 87 |
| R2010 | 80 | 67 | 82 | 79 |
| R2011 | 88 | 82 | 61 | 72 |
| R2012 | 74 | 76 | 61 | 50 |
| R2013 | 89 | 80 | 77 | 69 |
| R2014 | 75 | 75 | 72 | 75 |
| R2015 | 71 | 79 | 71 | 66 |
| R2017 | 82 | 91 | 87 | 72 |
| R2018 | 75 | 76 | 73 | 55 |
| R2019 | 66 | 67 | 56 | 56 |
| R2020 | 83 | 76 | 65 | 69 |
| Mean | 78.5 | 76.2 | 70.3 | 67.0 |
| SD | 11.15 | 11.21 | 12.21 | 10.18 |
| SE | 2.49 | 2.51 | 2.73 | 2.28 |

***TABLE 7A. HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY***

***TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 127 | 134 | 142 | 141 | 135 | 136 | 144 | 136 |
| R2001 | 125 | 130 | 118 | 124 | 136 | 128 | 123 | 122 |
| R2002 | 121 | 124 | 142 | 124 | 123 | 110 | 121 | 114 |
| R2003 | 122 | 120 | 129 | 120 | 125 | 118 | 128 | 131 |
| R2004 | 94 | 100 | 101 | 104 | 102 | 106 | 125 | 108 |
| R2005 | 141 | 145 | 147 | 133 | 114 | 111 | 105 | 106 |
| R2006 | 114 | 122 | 120 | 114 | 120 | 123 | 116 | 117 |
| R2007 | 139 | 136 | 142 | 129 | 135 | 135 | 133 | 141 |
| R2008 | 138 | 113 | 129 | 135 | 136 | 132 | 130 | 138 |
| R2009 | 143 | 138 | 150 | 143 | 144 | 154 | 161 | 150 |
| R2010 | 126 | 137 | 130 | 128 | 130 | 129 | 126 | 130 |
| R2011 | 117 | 135 | 148 | 129 | 139 | 129 | 131 | 145 |
| R2012 | 117 | 125 | 126 | 136 | 134 | 115 | 111 | 120 |
| R2013 | 126 | 127 | 124 | 138 | 113 | 118 | 131 | 123 |
| R2014 | 111 | 122 | 122 | 112 | 116 | 129 | 132 | 130 |
| R2015 | 122 | 133 | 117 | 117 | 118 | 133 | 137 | 142 |
| R2017 | 128 | 135 | 130 | 145 | 136 | 144 | 139 | 140 |
| R2018 | 130 | 131 | 129 | 133 | 132 | 133 | 128 | 132 |
| R2019 | 125 | 127 | 128 | 132 | 130 | 128 | 120 | 133 |
| R2020 | 138 | 135 | 138 | 138 | 132 | 133 | 141 | 136 |
| Mean | 125.2 | 128.4 | 130.6 | 128.7 | 127.5 | 127.1 | 128.9 | 129.7 |
| SD | 11.59 | 10.06 | 12.34 | 11.00 | 10.69 | 11.78 | 12.30 | 12.21 |
| SE | 2.59 | 2.25 | 2.76 | 2.46 | 2.39 | 2.63 | 2.75 | 2.73 |

***TABLE 7A. (CONTINUED) HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 137 | 147 | 153 | 139 |
| R2001 | 116 | 97 | 104 | 90 |
| R2002 | 109 | 106 | 111 | 112 |
| R2003 | 131 | 97 | 114 | 114 |
| R2004 | 102 | 98 | 96 | 84 |
| R2005 | 113 | 100 | 101 | |
| R2006 | 102 | 126 | 120 | 123 |
| R2007 | 140 | 138 | 138 | 145 |
| R2008 | 126 | 125 | 113 | 114 |
| R2009 | 145 | 149 | 144 | 136 |
| R2010 | 131 | 142 | 130 | 115 |
| R2011 | 137 | 125 | 128 | 115 |
| R2012 | 128 | 109 | 98 | 102 |
| R2013 | 125 | 122 | 115 | 108 |
| R2014 | 134 | | | |
| R2015 | 141 | 128 | 138 | 105 |
| R2017 | 128 | 113 | 106 | 110 |
| R2018 | 152 | 136 | 139 | 138 |
| R2019 | 120 | 132 | 123 | 107 |
| R2020 | 137 | 131 | 127 | 135 |
| Mean | 127.6 | 122.0 | 120.8 | 116.1 |
| SD | 13.95 | 17.14 | 16.56 | 16.91 |
| SE | 3.12 | 3.83 | 3.70 | 3.78 |

***TABLE 7B. HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY***

***TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 83 | 84 | 88 | 76 | 82 | 78 | 82 | 77 |
| R2001 | 87 | 93 | 71 | 75 | 90 | 80 | 72 | 74 |
| R2002 | 89 | 77 | 94 | 84 | 83 | 81 | 79 | 71 |
| R2003 | 88 | 89 | 90 | 82 | 82 | 87 | 87 | 88 |
| R2004 | 56 | 61 | 54 | 60 | 54 | 63 | 68 | 66 |
| R2005 | 78 | 76 | 82 | 69 | 51 | 53 | 49 | 59 |
| R2006 | 74 | 77 | 77 | 71 | 72 | 78 | 67 | 74 |
| R2007 | 92 | 94 | 92 | 88 | 94 | 93 | 89 | 94 |
| R2008 | 82 | 65 | 74 | 79 | 84 | 80 | 80 | 72 |
| R2009 | 92 | 90 | 101 | 92 | 94 | 106 | 99 | 99 |
| R2010 | 83 | 81 | 71 | 82 | 77 | 72 | 78 | 85 |
| R2011 | 82 | 75 | 77 | 83 | 78 | 84 | 86 | 78 |
| R2012 | 79 | 75 | 82 | 82 | 94 | 80 | 69 | 74 |
| R2013 | 74 | 77 | 78 | 81 | 63 | 77 | 83 | 75 |
| R2014 | 77 | 79 | 77 | 75 | 75 | 87 | 78 | 85 |
| R2015 | 78 | 73 | 68 | 71 | 71 | 73 | 72 | 79 |
| R2017 | 74 | 77 | 80 | 68 | 81 | 80 | 86 | 80 |
| R2018 | 79 | 63 | 67 | 70 | 69 | 72 | 76 | 77 |
| R2019 | 72 | 68 | 74 | 82 | 75 | 78 | 78 | 74 |
| R2020 | 82 | 76 | 76 | 88 | 78 | 80 | 90 | 90 |
| Mean | 80.0 | 77.4 | 78.5 | 77.9 | 77.3 | 79.0 | 78.3 | 78.4 |
| SD | 8.10 | 9.18 | 10.74 | 8.10 | 11.95 | 10.67 | 10.64 | 9.43 |
| SE | 1.81 | 2.05 | 2.40 | 1.81 | 2.67 | 2.38 | 2.38 | 2.11 |

***TABLE 7B. (CONTINUED) HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 80 | 86 | 90 | 89 |
| R2001 | 68 | 44 | 59 | 52 |
| R2002 | 67 | 69 | 71 | 76 |
| R2003 | 85 | 75 | 71 | 82 |
| R2004 | 54 | 53 | 49 | 43 |
| R2005 | 61 | 52 | 52 | |
| R2006 | 64 | 79 | 74 | 72 |
| R2007 | 89 | 90 | 92 | 94 |
| R2008 | 70 | 77 | 64 | 69 |
| R2009 | 95 | 97 | 93 | 86 |
| R2010 | 78 | 86 | 76 | 64 |
| R2011 | 74 | 72 | 71 | 67 |
| R2012 | 82 | 65 | 59 | 64 |
| R2013 | 70 | 75 | 79 | 63 |
| R2014 | 87 | | | |
| R2015 | 77 | 75 | 76 | 48 |
| R2017 | 76 | 59 | 66 | 55 |
| R2018 | 79 | 64 | 68 | 65 |
| R2019 | 77 | 75 | 71 | 54 |
| R2020 | 86 | 82 | 81 | 83 |
| Mean | 75.9 | 72.4 | 71.6 | 68.0 |
| SD | 10.05 | 13.72 | 12.36 | 14.68 |
| SE | 2.25 | 3.07 | 2.76 | 3.28 |

***TABLE 8A. HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY***

***TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 135 | 130 | 140 | 130 | 142 | 145 | 141 | 150 |
| R2001 | 140 | 137 | 137 | 139 | 127 | 125 | 121 | 131 |
| R2002 | 123 | 128 | 131 | 128 | 127 | 129 | 126 | 130 |
| R2003 | 121 | 136 | 131 | 122 | 117 | 113 | 125 | 124 |
| R2004 | 109 | 109 | 109 | 117 | 119 | 118 | 110 | 124 |
| R2005 | 138 | 137 | 135 | 125 | 138 | 134 | 137 | 136 |
| R2006 | 118 | 123 | 132 | 124 | 124 | 126 | 128 | 119 |
| R2007 | 113 | 124 | 127 | 127 | 111 | 117 | 119 | 122 |
| R2008 | 127 | 122 | 121 | 128 | 145 | 146 | 138 | 131 |
| R2009 | 132 | 135 | 135 | 152 | 150 | 153 | 161 | 153 |
| R2010 | 123 | 121 | 137 | 136 | 120 | 118 | 131 | 134 |
| R2011 | 132 | 119 | 135 | 132 | 129 | 136 | 136 | 128 |
| R2012 | 127 | 119 | 125 | 120 | 130 | 132 | 125 | 127 |
| R2013 | 127 | 131 | 128 | 136 | 126 | 137 | 131 | 137 |
| R2014 | 118 | 122 | 120 | 117 | 132 | 122 | 126 | 138 |
| R2015 | 114 | 115 | 113 | 115 | 120 | 131 | 125 | 106 |
| R2017 | 131 | 154 | 134 | 126 | 136 | 136 | 136 | 130 |
| R2018 | 110 | 132 | 132 | 123 | 127 | 133 | 142 | 141 |
| R2019 | 123 | 115 | 123 | 119 | 118 | 121 | 132 | 129 |
| R2020 | 136 | 140 | 133 | 139 | 143 | 144 | 146 | 139 |
| Mean | 124.8 | 127.5 | 128.8 | 127.7 | 128.9 | 130.6 | 131.8 | 131.4 |
| SD | 9.27 | 10.64 | 8.27 | 9.10 | 10.56 | 10.92 | 10.97 | 10.51 |
| SE | 2.07 | 2.38 | 1.85 | 2.04 | 2.36 | 2.44 | 2.45 | 2.35 |

***TABLE 8A. (CONTINUED) HOURLY SYSTOLIC BLOOD PRESSURE FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 140 | 148 | 138 | 102 |
| R2001 | 110 | 115 | 115 | 120 |
| R2002 | 137 | 133 | 124 | 122 |
| R2003 | 146 | 126 | 124 | 94 |
| R2004 | 143 | 123 | 126 | 104 |
| R2005 | 135 | 133 | 120 | 106 |
| R2006 | 125 | 129 | 142 | 129 |
| R2007 | 119 | 117 | 122 | 129 |
| R2008 | 125 | 117 | 134 | 133 |
| R2009 | 150 | 145 | 138 | 140 |
| R2010 | 130 | 136 | 137 | 138 |
| R2011 | 131 | 128 | 118 | 111 |
| R2012 | 118 | 120 | 109 | 94 |
| R2013 | 135 | 132 | 129 | 117 |
| R2014 | 135 | 126 | 124 | 122 |
| R2015 | 112 | 129 | 124 | 120 |
| R2017 | 114 | 113 | 111 | 117 |
| R2018 | 130 | 121 | 123 | 122 |
| R2019 | 131 | 131 | 124 | 115 |
| R2020 | 138 | 124 | 130 | 120 |
| Mean | 130.2 | 127.3 | 125.7 | 117.7 |
| SD | 11.29 | 9.29 | 8.81 | 13.09 |
| SE | 2.53 | 2.08 | 1.97 | 2.93 |

***TABLE 8B. HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 94 | 95 | 88 | 78 | 84 | 80 | 86 | 93 |
| R2001 | 77 | 70 | 75 | 76 | 73 | 80 | 76 | 68 |
| R2002 | 82 | 82 | 83 | 84 | 81 | 81 | 81 | 81 |
| R2003 | 90 | 87 | 97 | 89 | 78 | 90 | 89 | 87 |
| R2004 | 63 | 53 | 54 | 63 | 65 | 70 | 58 | 66 |
| R2005 | 76 | 69 | 68 | 62 | 80 | 74 | 76 | 73 |
| R2006 | 78 | 73 | 75 | 72 | 73 | 73 | 81 | 77 |
| R2007 | 83 | 83 | 81 | 89 | 71 | 79 | 84 | 87 |
| R2008 | 80 | 73 | 78 | 74 | 79 | 87 | 80 | 72 |
| R2009 | 84 | 89 | 85 | 100 | 91 | 93 | 90 | 90 |
| R2010 | 81 | 84 | 80 | 73 | 77 | 76 | 79 | 86 |
| R2011 | 76 | 84 | 87 | 73 | 73 | 84 | 88 | 73 |
| R2012 | 84 | 78 | 80 | 78 | 86 | 87 | 80 | 79 |
| R2013 | 82 | 89 | 83 | 87 | 81 | 90 | 80 | 94 |
| R2014 | 76 | 72 | 75 | 73 | 89 | 85 | 79 | 84 |
| R2015 | 68 | 67 | 60 | 70 | 70 | 72 | 68 | 67 |
| R2017 | 86 | 87 | 92 | 80 | 83 | 90 | 82 | 75 |
| R2018 | 69 | 75 | 80 | 71 | 67 | 76 | 80 | 75 |
| R2019 | 70 | 65 | 70 | 72 | 68 | 69 | 76 | 72 |
| R2020 | 91 | 89 | 85 | 78 | 92 | 90 | 77 | 90 |
| Mean | 79.4 | 78.1 | 78.7 | 76.9 | 77.9 | 81.2 | 79.4 | 79.5 |
| SD | 8.03 | 10.43 | 10.11 | 8.96 | 8.10 | 7.42 | 7.08 | 8.90 |
| SE | 1.79 | 2.33 | 2.26 | 2.00 | 1.81 | 1.66 | 1.58 | 1.99 |

***TABLE 8B. (CONTINUED) HOURLY DIASTOLIC BLOOD PRESSURE FOLLOWING A CONTINUOUS PHYISCAL ACTIVITY TREATMENT***

| | Hourly Mean Blood Pressure (mm Hg) Following a Treatment | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 88 | 82 | 82 | 60 |
| R2001 | 49 | 58 | 60 | 41 |
| R2002 | 86 | 89 | 83 | 85 |
| R2003 | 90 | 90 | 81 | 59 |
| R2004 | 69 | 63 | 70 | 64 |
| R2005 | 78 | 84 | 62 | 56 |
| R2006 | 79 | 77 | 87 | 72 |
| R2007 | 77 | 80 | 81 | 91 |
| R2008 | 66 | 68 | 77 | 80 |
| R2009 | 93 | 95 | 83 | 87 |
| R2010 | 89 | 86 | 77 | 78 |
| R2011 | 70 | 75 | 79 | 69 |
| R2012 | 76 | 80 | 73 | 59 |
| R2013 | 85 | 89 | 83 | 75 |
| R2014 | 88 | 78 | 77 | 76 |
| R2015 | 67 | 72 | 65 | 64 |
| R2017 | 59 | 61 | 58 | 62 |
| R2018 | 78 | 64 | 65 | 53 |
| R2019 | 77 | 69 | 72 | 60 |
| R2020 | 86 | 83 | 76 | 74 |
| Mean | 77.3 | 77.1 | 74.5 | 68.2 |
| SD | 11.49 | 10.50 | 8.58 | 12.70 |
| SE | 2.57 | 2.35 | 1.92 | 2.84 |

***TABLE 9. AMBULATORY BLOOD PRESSURE MONITORING FOR REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | | ***Baseline*** | | | | ***1st session*** | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **Starting Time** | **Sampled** | **Used** | **% Edited** | **Starting Time** | **Sampled** | **Used** | **% Edited** |
| R2000 | 8:35 | 3 | 3 | 100.0 | 9:08 | 6 | 6 | 100.0 |
| R2001 | 9:32 | 3 | 3 | 100.0 | 10:03 | 7 | 7 | 100.0 |
| R2002 | 9:21 | 3 | 3 | 100.0 | 9:48 | 7 | 7 | 100.0 |
| R2003 | 9:03 | 3 | 3 | 100.0 | 9:36 | 7 | 7 | 100.0 |
| R2004 | 8:57 | 3 | 3 | 100.0 | 9:42 | 6 | 6 | 100.0 |
| R2005 | 9:01 | 3 | 3 | 100.0 | 9:31 | 7 | 7 | 100.0 |
| R2007 | 8:56 | 3 | 3 | 100.0 | 9:25 | 7 | 7 | 100.0 |
| R2008 | 8:23 | 3 | 3 | 100.0 | 8:57 | 7 | 7 | 100.0 |
| R2009 | 8:48 | 3 | 3 | 100.0 | 9:15 | 7 | 7 | 100.0 |
| R2010 | 8:53 | 3 | 3 | 100.0 | 9:22 | 7 | 7 | 100.0 |
| R2011 | 8:57 | 3 | 3 | 100.0 | 9:37 | 7 | 7 | 100.0 |
| R2012 | 9:20 | 3 | 3 | 100.0 | 9:57 | 7 | 7 | 100.0 |
| R2013 | 8:50 | 3 | 3 | 100.0 | 9:17 | 7 | 7 | 100.0 |
| R2014 | 8:59 | 3 | 3 | 100.0 | 9:28 | 7 | 7 | 100.0 |
| R2015 | 8:52 | 3 | 3 | 100.0 | 9:18 | 6 | 6 | 100.0 |
| R2016 | 8:43 | 3 | 3 | 100.0 | 9:13 | 7 | 7 | 100.0 |
| R2017 | 9:18 | 3 | 3 | 100.0 | 9:47 | 7 | 7 | 100.0 |
| R2018 | 8:58 | 3 | 3 | 100.0 | 9:26 | 7 | 7 | 100.0 |
| R2019 | 9:19 | 3 | 3 | 100.0 | 9:51 | 7 | 7 | 100.0 |
| R2020 | 9:32 | 3 | 3 | 100.0 | 10:02 | 7 | 7 | 100.0 |
| Mean | 9:00 | 3.0 | 3.0 | 100.0 | 9:32 | 6.9 | 6.9 | 100.0 |
| S.D. | 0:17 | 0.00 | 0.00 | 0.00 | 0:18 | 0.37 | 0.37 | 0.00 |
| S.E. | 0:03 | 0.00 | 0.00 | 0.00 | 0:04 | 0.08 | 0.08 | 0.00 |

***TABLE 9. (CONTINUED) AMBULATORY BLOOD PRESSURE MONITORING FOR AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | | *2nd session* | | | | *3rd session* | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **Starting Time** | **Sampled** | **Used** | **% Edited** | **Starting Time** | **Sampled** | **Used** | **% Edited** |
| R2000 | 9:59 | 6 | 6 | 100.0 | 10:59 | 3 | 3 | 100.0 |
| R2001 | 11:06 | 7 | 7 | 100.0 | 12:07 | 5 | 5 | 100.0 |
| R2002 | 10:48 | 7 | 7 | 100.0 | 11:49 | 7 | 7 | 100.0 |
| R2003 | 10:37 | 5 | 5 | 100.0 | 11:39 | 7 | 7 | 100.0 |
| R2004 | 10:43 | 7 | 7 | 100.0 | 11:45 | 7 | 7 | 100.0 |
| R2005 | 10:31 | 7 | 7 | 100.0 | 11:31 | 6 | 6 | 100.0 |
| R2007 | 10:24 | 7 | 7 | 100.0 | 11:23 | 7 | 7 | 100.0 |
| R2008 | 9:57 | 7 | 7 | 100.0 | 10:59 | 7 | 7 | 100.0 |
| R2009 | 10:15 | 7 | 7 | 100.0 | 11:15 | 7 | 7 | 100.0 |
| R2010 | 10:22 | 7 | 7 | 100.0 | 11:22 | 7 | 7 | 100.0 |
| R2011 | 10:37 | 7 | 7 | 100.0 | 11:37 | 7 | 7 | 100.0 |
| R2012 | 10:53 | 6 | 6 | 100.0 | 11:53 | 7 | 7 | 100.0 |
| R2013 | 10:19 | 7 | 7 | 100.0 | 11:19 | 7 | 7 | 100.0 |
| R2014 | 10:29 | 7 | 7 | 100.0 | 11:28 | 6 | 6 | 100.0 |
| R2015 | 10:19 | 7 | 7 | 100.0 | 11:19 | 7 | 7 | 100.0 |
| R2016 | 10:13 | 7 | 7 | 100.0 | 11:13 | 7 | 7 | 100.0 |
| R2017 | 10:47 | 7 | 7 | 100.0 | 11:47 | 7 | 7 | 100.0 |
| R2018 | 10:26 | 7 | 7 | 100.0 | 11:30 | 6 | 6 | 100.0 |
| R2019 | 10:51 | 7 | 7 | 100.0 | 11:52 | 7 | 7 | 100.0 |
| R2020 | 11:03 | 7 | 7 | 100.0 | 12:03 | 6 | 6 | 100.0 |
| Mean | 10:31 | 6.80 | 6.80 | 100.0 | 11:32 | 6.50 | 6.50 | 100.0 |
| S.D. | 0:18 | 0.52 | 0.52 | 0.00 | 0:18 | 1.00 | 1.00 | 0.00 |
| S.E. | 0:04 | 0.12 | 0.12 | 0.00 | 0:04 | 0.22 | 0.22 | 0.00 |

***TABLE 10A. SYSTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | ***Baseline Systolic Blood Pressure (mm Hg)*** | | | | | ***Systolic Blood Pressure Following the 1st Short Session (mm Hg)*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **Mean** | | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 152 | 129 | 134 | 138.3 | | 153 | 133 | 133 | 144 | 130 | 128 | | 136.8 |
| R2001 | 136 | 122 | 119 | 125.6 | | 126 | 118 | 124 | 129 | 126 | 124 | 121 | 124.0 |
| R2002 | 124 | 120 | 129 | 124.3 | | 123 | 124 | 125 | 149 | 119 | 121 | 109 | 122.3 |
| R2003 | 127 | 129 | 126 | 127.3 | | 127 | 124 | 123 | 123 | 121 | 118 | 120 | 124.3 |
| R2004 | 117 | 108 | 107 | 110.7 | | 124 | 107 | 95 | 107 | 111 | 92 | | 106.0 |
| R2005 | 149 | 137 | 145 | 143.6 | | 144 | 144 | 139 | 136 | 140 | 131 | 128 | 137.4 |
| R2007 | 125 | 129 | 125 | 126.3 | | 123 | 120 | 125 | 125 | 125 | 136 | 139 | 127.6 |
| R2008 | 115 | 114 | 124 | 117.6 | | 132 | 135 | 118 | 118 | 117 | 113 | 120 | 121.9 |
| R2009 | 148 | 150 | 134 | 144.0 | | 144 | 148 | 144 | 143 | 138 | 150 | 145 | 144.6 |
| R2010 | 130 | 128 | 128 | 128.6 | | 135 | 128 | 136 | 136 | 126 | 134 | 140 | 133.6 |
| R2011 | 116 | 125 | 129 | 123.3 | | 129 | 107 | 102 | 112 | 110 | 110 | 108 | 111.1 |
| R2012 | 120 | 121 | 108 | 116.3 | | 117 | 104 | 117 | 122 | 118 | 112 | 115 | 115.0 |
| R2013 | 123 | 134 | 136 | 131.0 | | 130 | 119 | 122 | 131 | 122 | 127 | 129 | 125.7 |
| R2014 | 128 | 121 | 122 | 123.7 | | | 122 | 124 | 128 | 122 | 122 | 124 | 123.7 |
| R2015 | 110 | 98 | 103 | 103.7 | | 117 | 94 | 91 | 100 | 107 | 115 | 110 | 104.9 |
| R2016 | 134 | 132 | 132 | 132.7 | | 136 | 136 | 129 | 139 | 137 | 136 | 128 | 134.4 |
| R2017 | 122 | 126 | 119 | 122.3 | | 129 | 123 | 123 | 126 | 116 | 121 | 126 | 123.4 |
| R2018 | 121 | 133 | 120 | 124.7 | | 129 | 123 | 125 | 125 | 110 | 117 | 121 | 121.4 |
| R2019 | 130 | 119 | 121 | 123.3 | | 125 | 120 | 123 | 126 | 111 | 115 | 113 | 119.0 |
| R2020 | 147 | 146 | 139 | 144.0 | | 149 | 144 | 143 | 139 | 140 | 141 | 130 | 140.9 |
| Mean | 128.7 | 126.1 | 125.0 | 126.6 | | 131.2 | 123.7 | 123.1 | 127.9 | 122.3 | 123.2 | 123.7 | 124.9 |
| SD | 12.2 | 11.9 | 10.7 | 10.56 | | 10.13 | 13.98 | 14.01 | 12.50 | 10.45 | 12.91 | 10.70 | 10.83 |
| SE | | | | 2.36 | | | | | | | | | 2.42 |

***TABLE 10A. (CONTINUED) SYSTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSONS OF PHYSICAL ACTIVITY TREATMENT***

| | *Systolic Blood Pressure Following the 2nd Short Session (mm Hg)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 129 | 128 | 132 | 129 | 122 | 127 | | 127.8 |
| R2001 | 118 | 122 | 127 | 121 | 121 | 119 | 119 | 121.0 |
| R2002 | 116 | 129 | 125 | 116 | 113 | 126 | 118 | 120.4 |
| R2003 | 125 | 124 | 118 | 122 | | | 118 | 121.4 |
| R2004 | 92 | 93 | 87 | 99 | 94 | 93 | 89 | 92.4 |
| R2005 | 150 | 154 | 145 | 131 | 130 | 131 | 131 | 138.9 |
| R2007 | 128 | 124 | 145 | 127 | 130 | 128 | 123 | 129.3 |
| R2008 | 119 | 137 | 129 | 135 | 128 | 117 | 117 | 126.0 |
| R2009 | 138 | 146 | 135 | 138 | 136 | 139 | 148 | 140.0 |
| R2010 | 135 | 132 | 136 | 130 | 127 | 117 | 122 | 128.4 |
| R2011 | | 128 | 115 | 121 | 109 | 120 | 114 | 117.8 |
| R2012 | 124 | 132 | 115 | 121 | 109 | 122 | 128 | 121.6 |
| R2013 | 130 | 99 | 118 | 125 | 114 | 112 | 115 | 116.1 |
| R2014 | 113 | 123 | 117 | 125 | 125 | 122 | 127 | 121.7 |
| R2015 | 115 | 118 | 119 | 119 | 109 | 119 | 108 | 115.3 |
| R2016 | 143 | 139 | 125 | 120 | 126 | 126 | 125 | 129.1 |
| R2017 | 128 | 119 | 121 | 118 | 126 | 127 | 125 | 123.4 |
| R2018 | 125 | 130 | 126 | 120 | 126 | 122 | 120 | 124.1 |
| R2019 | 125 | 133 | 118 | 125 | 111 | 120 | 112 | 120.6 |
| R2020 | 144 | 130 | 146 | 147 | 137 | 141 | 143 | 141.1 |
| Mean | 126.2 | 127.0 | 125.0 | 124.5 | 120.7 | 122.5 | 121.2 | 123.8 |
| SD | 13.15 | 13.74 | 13.45 | 9.67 | 11.04 | 10.17 | 12.54 | 10.48 |
| SE | | | | | | | | 2.34 |

***TABLE 10A. (CONTINUED) SYSTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | ***Systolic Blood Pressure Following the 3rd Short Session (mm Hg)*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 130 | 138 | 138 | | | | | 135.3 |
| R2001 | 122 | 124 | 115 | 125 | 117 | | | 120.6 |
| R2002 | 120 | 122 | 122 | 112 | 109 | 120 | 121 | 118.0 |
| R2003 | 120 | 130 | 109 | 98 | 119 | 109 | 113 | 114.0 |
| R2004 | 110 | 102 | 104 | 105 | 70 | 100 | 100 | 98.7 |
| R2005 | 137 | 126 | 137 | 127 | 126 | 122 | | 129.2 |
| R2007 | 136 | 124 | 121 | 122 | 128 | 125 | 127 | 126.1 |
| R2008 | 122 | 112 | 120 | 125 | 129 | 123 | 128 | 122.7 |
| R2009 | 142 | 138 | 139 | 132 | 138 | 128 | 137 | 136.3 |
| R2010 | 130 | 117 | 123 | 121 | 122 | 129 | 116 | 122.6 |
| R2011 | 93 | 115 | 103 | 111 | 107 | 98 | 106 | 104.7 |
| R2012 | 117 | 126 | 122 | 120 | 127 | 118 | 125 | 122.1 |
| R2013 | 124 | 122 | 121 | 128 | 119 | 121 | | 122.5 |
| R2014 | 126 | 120 | 120 | 125 | 121 | 128 | 130 | 124.3 |
| R2015 | 115 | 115 | 113 | 97 | 118 | 115 | 108 | 111.6 |
| R2016 | 138 | 129 | 135 | 132 | 122 | 133 | 125 | 130.6 |
| R2017 | 129 | 127 | 131 | 129 | 125 | 125 | 126 | 127.4 |
| R2018 | | 128 | 130 | 120 | 120 | 127 | 122 | 124.5 |
| R2019 | 125 | 124 | 122 | 124 | 127 | | 117 | 123.2 |
| R2020 | 140 | 140 | 149 | 138 | 143 | 146 | 142 | 142.6 |
| Mean | 125.1 | 124.0 | 123.7 | 120.6 | 120.4 | 121.6 | 121.4 | 122.9 |
| SD | 11.78 | 9.19 | 12.03 | 11.25 | 14.85 | 11.61 | 11.13 | 10.28 |
| SE | | | | | | | | 2.30 |

***TABLE 10B. DIASTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | ***Baseline Diastolic Blood Pressure*** | | | | | ***Diastolic Blood Pressure Following the 1st Short Session*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **Mean** | | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 99 | 88 | 93 | 93.3 | | 97 | 95 | 96 | 91 | 89 | | | 93.6 |
| R2001 | 87 | 72 | 91 | 83.3 | | 82 | 86 | 78 | 75 | | 81 | 92 | 82.3 |
| R2002 | 98 | 97 | 92 | 95.7 | | 95 | 91 | 88 | 94 | 91 | 85 | 95 | 91.3 |
| R2003 | 89 | 93 | 90 | 90.7 | | 95 | 94 | 93 | 87 | 97 | 86 | 91 | 91.9 |
| R2004 | 65 | 67 | 69 | 67.0 | | 63 | 50 | 51 | 44 | 59 | 45 | | 52.0 |
| R2005 | 80 | 75 | 81 | 78.7 | | 95 | 83 | 88 | 68 | 95 | 77 | 81 | 83.9 |
| R2007 | 85 | 93 | 90 | 89.3 | | 93 | 90 | 86 | 87 | 86 | 95 | 97 | 90.6 |
| R2008 | 75 | 63 | 67 | 68.3 | | 82 | 73 | 72 | 75 | 78 | 81 | 82 | 77.6 |
| R2009 | 92 | 92 | 88 | 90.7 | | 99 | 100 | 104 | 101 | 93 | 100 | 98 | 99.3 |
| R2010 | 86 | 77 | 79 | 80.7 | | 76 | 77 | 70 | 81 | 75 | 78 | 77 | 76.3 |
| R2011 | 78 | 83 | 72 | 77.7 | | 72 | 70 | 68 | 74 | 70 | 68 | 73 | 70.7 |
| R2012 | 77 | 79 | 76 | 77.3 | | 76 | 82 | 81 | 82 | 80 | 76 | 78 | 79.3 |
| R2013 | 76 | 84 | 85 | 81.7 | | 87 | 78 | 81 | 83 | 90 | 89 | 83 | 84.4 |
| R2014 | 83 | 87 | 81 | 83.7 | | | 87 | 87 | 87 | 86 | 82 | 91 | 86.7 |
| R2015 | 66 | 72 | 70 | 69.3 | | 79 | 68 | 67 | 64 | 72 | 75 | 70 | 70.7 |
| R2016 | 76 | 75 | 69 | 73.3 | | 70 | 70 | 78 | 75 | 71 | 85 | 76 | 75.0 |
| R2017 | 81 | 81 | 81 | 81.0 | | 78 | 84 | 84 | 83 | 79 | 84 | 78 | 81.4 |
| R2018 | 69 | 72 | 72 | 71.0 | | 75 | 78 | 78 | 76 | 78 | 81 | 74 | 77.1 |
| R2019 | 84 | 80 | 76 | 80.0 | | 84 | 69 | 86 | 82 | 67 | 79 | 76 | 77.6 |
| R2020 | 84 | 86 | 89 | 86.3 | | 88 | 88 | 90 | 96 | 89 | 92 | 85 | 89.7 |
| Mean | 81.5 | 80.8 | 80.55 | 81.0 | | 83.5 | 80.7 | 81.3 | 80.3 | 81.3 | 81.0 | 83.2 | 81.6 |
| SD | 9.26 | 9.30 | 8.80 | 8.42 | | 10.32 | 11.79 | 11.84 | 12.59 | 10.53 | 11.46 | 8.80 | 10.47 |
| SE | | | | 1.88 | | | | | | | | | 2.34 |

***TABLE 10B. (CONTINUED) DIASTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | ***Diastolic Blood Pressure Following the 2nd Short Session*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 87 | 90 | 86 | 94 | 88 | 102 | 87 | 90.6 |
| R2001 | 79 | 78 | 83 | 76 | 76 | 84 | 77 | 79.0 |
| R2002 | 84 | 96 | 92 | 77 | 87 | 87 | 88 | 87.3 |
| R2003 | 90 | 84 | 89 | 93 | | | 86 | 88.4 |
| R2004 | 51 | 55 | 50 | 54 | 64 | 58 | 63 | 56.4 |
| R2005 | 95 | 94 | 85 | 84 | 75 | 85 | 80 | 85.4 |
| R2007 | 93 | 97 | 99 | 87 | 91 | 85 | 90 | 91.7 |
| R2008 | 85 | 89 | 91 | 90 | 78 | 83 | 80 | 85.1 |
| R2009 | 94 | 93 | 83 | 98 | 102 | 94 | 98 | 94.6 |
| R2010 | 75 | 85 | 84 | 92 | 82 | 73 | 79 | 81.4 |
| R2011 | | 80 | 64 | 76 | 71 | 75 | 74 | 73.3 |
| R2012 | 84 | 88 | 79 | 80 | 82 | 87 | 88 | 84.0 |
| R2013 | 87 | 74 | 80 | 92 | 82 | 76 | 78 | 81.3 |
| R2014 | 80 | 85 | 82 | 81 | 82 | 87 | 85 | 83.1 |
| R2015 | 74 | 79 | 80 | 72 | 74 | 68 | 65 | 73.1 |
| R2016 | 73 | 96 | 74 | 76 | 82 | 70 | 70 | 77.3 |
| R2017 | 75 | 77 | 77 | 87 | 77 | 78 | 81 | 78.9 |
| R2018 | 82 | 82 | 80 | 76 | 85 | 80 | 81 | 80.9 |
| R2019 | 86 | 80 | 87 | 84 | 74 | 78 | 77 | 80.9 |
| R2020 | 92 | 94 | 92 | 92 | 96 | 85 | 95 | 92.3 |
| Mean | 82.4 | 84.0 | 81.9 | 83.1 | 81.5 | 80.8 | 81.1 | 82.3 |
| SD | 10.26 | 9.98 | 10.59 | 10.21 | 8.95 | 9.84 | 9.00 | 8.52 |
| SE | | | | | | | | 1.90 |

***TABLE 10B. (CONTINUED) DIASTOLIC BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHSYCIAL ACTIVITY TREATMENT***

| | ***Diastolic Blood Pressure Following the 3rd Short Session*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **5 min** | **10 min** | **15 min** | **20 min** | **30 min** | **40 min** | **50 min** | **Mean** |
| R2000 | 92 | 93 | 88 | | | | | 91.0 |
| R2001 | 78 | 75 | 82 | 78 | 73 | 88 | 94 | 81.1 |
| R2002 | 84 | 89 | 83 | 86 | 83 | 84 | 84 | 84.7 |
| R2003 | 90 | 89 | 79 | 80 | 89 | 82 | 92 | 85.9 |
| R2004 | 41 | 68 | 63 | 58 | 62 | 58 | 67 | 59.6 |
| R2005 | 86 | 75 | 82 | 81 | | 91 | 84 | 83.2 |
| R2007 | 92 | 89 | 91 | 90 | 97 | 92 | 91 | 91.7 |
| R2008 | 72 | 81 | 73 | 77 | 82 | 77 | 75 | 76.7 |
| R2009 | 92 | 96 | 92 | 88 | 100 | 93 | 104 | 95.0 |
| R2010 | 77 | 81 | 86 | 78 | 87 | 88 | 80 | 82.4 |
| R2011 | 73 | 68 | 67 | 76 | 71 | 58 | 74 | 69.6 |
| R2012 | 81 | 83 | 82 | 81 | 84 | 83 | 84 | 82.6 |
| R2013 | 76 | 84 | 81 | 82 | 85 | 92 | 84 | 83.4 |
| R2014 | 85 | 83 | 82 | 82 | 84 | 85 | 86 | 83.9 |
| R2015 | 70 | 74 | 77 | 70 | 79 | 71 | 71 | 73.1 |
| R2016 | 80 | 74 | 71 | 78 | 78 | 85 | 75 | 77.3 |
| R2017 | 76 | 78 | 79 | 78 | 82 | 79 | 82 | 79.1 |
| R2018 | | 77 | 84 | 84 | 77 | 76 | 73 | 78.5 |
| R2019 | 82 | 82 | 78 | 78 | 79 | | 70 | 78.2 |
| R2020 | 92 | 93 | 92 | 88 | 92 | 84 | 96 | 91.0 |
| Mean | 80.0 | 81.6 | 80.6 | 79.6 | 82.4 | 81.4 | 82.4 | 81.4 |
| SD | 11.87 | 8.11 | 7.77 | 7.14 | 9.07 | 10.40 | 9.92 | 8.17 |
| SE | | | | | | | | 1.83 |

***TABLE 11. BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY TREATMENT***

| | ***Systolic Blood Pressure (mm Hg)*** | | | |
|---|---|---|---|---|
| **ID** | **Baseline** | **1st** | **2nd** | **3rd** |
| R2000 | 138 | 134 | 128 | 138 |
| R2001 | 126 | 124 | 122 | 120 |
| R2002 | 127 | 122 | 121 | 113 |
| R2003 | 124 | 125 | 121 | 118 |
| R2004 | 111 | 102 | 93 | 97 |
| R2005 | 144 | 136 | 137 | 128 |
| R2007 | 126 | 128 | 130 | 125 |
| R2008 | 118 | 120 | 127 | 123 |
| R2009 | 144 | 145 | 140 | 135 |
| R2010 | 129 | 133 | 127 | 121 |
| R2011 | 123 | 108 | 118 | 107 |
| R2012 | 116 | 115 | 121 | 123 |
| R2013 | 131 | 125 | 114 | 122 |
| R2014 | 124 | 124 | 123 | 124 |
| R2015 | 104 | 103 | 115 | 111 |
| R2016 | 133 | 134 | 127 | 129 |
| R2017 | 122 | 123 | 123 | 127 |
| R2018 | 125 | 120 | 124 | 125 |
| R2019 | 123 | 118 | 120 | 123 |
| R2020 | 144 | 140 | 141 | 143 |
| Mean | 126.6 | 123.9 | 123.5 | 122.6 |
| SD | 10.56 | 11.35 | 10.37 | 10.49 |
| SE | 2.36 | 2.54 | 2.32 | 2.35 |

Values of blood pressure were average for 15-minute baseline and the last 40 minutes of rest period following successive short sessions of exercise treatment.

***TABLE 11. (CONTINUED) BLOOD PRESSURES FOR BASELINE AND REST PERIOD BETWEEN SHORT SESSIONS OF PHYSICAL ACTIVITY***

***TREATMENT***

| | *Diastolic Blood Pressure (mm Hg)* | | | |
|---|---|---|---|---|
| **ID** | **Baseline** | **1st** | **2nd** | **3rd** |
| R2000 | 93 | 93 | 91 | 91 |
| R2001 | 83 | 82 | 79 | 82 |
| R2002 | 91 | 91 | 88 | 85 |
| R2003 | 96 | 91 | 88 | 85 |
| R2004 | 67 | 50 | 57 | 63 |
| R2005 | 79 | 82 | 84 | 83 |
| R2007 | 89 | 90 | 92 | 92 |
| R2008 | 68 | 77 | 85 | 78 |
| R2009 | 91 | 99 | 95 | 96 |
| R2010 | 81 | 76 | 83 | 83 |
| R2011 | 78 | 71 | 73 | 69 |
| R2012 | 77 | 80 | 84 | 83 |
| R2013 | 82 | 84 | 80 | 85 |
| R2014 | 84 | 87 | 84 | 84 |
| R2015 | 69 | 69 | 73 | 74 |
| R2016 | 73 | 76 | 78 | 77 |
| R2017 | 81 | 82 | 80 | 80 |
| R2018 | 71 | 78 | 81 | 79 |
| R2019 | 80 | 77 | 80 | 77 |
| R2020 | 86 | 90 | 92 | 91 |
| Mean | 93 | 81.19 | 82.29 | 81.6 |
| SD | 8.42 | 10.77 | 8.38 | 7.79 |
| SE | 1.88 | 2.41 | 1.87 | 1.74 |

Values of blood pressure were average for 15-minute baseline and the last 40 minutes of rest period following successive short sessions of exercise treatment.

***TABLE 12A. CUMULATIVE SUM OF SYSTOLIC BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 17 | 9 | 18 | 1 | 2 | -14 | -10 | 9 |
| R2001 | 5 | 14 | 22 | 8 | 2 | 6 | 10 | 4 |
| R2002 | 18 | 15 | -7 | 11 | 12 | 24 | 18 | 15 |
| R2003 | 0 | 17 | -9 | 5 | 7 | 17 | 6 | -3 |
| R2004 | 27 | 17 | -3 | 8 | 5 | 3 | -10 | -1 |
| R2005 | 25 | 18 | 24 | 21 | 46 | 20 | 23 | 28 |
| R2006 | 8 | 3 | 13 | 20 | 1 | 6 | 4 | -8 |
| R2007 | 1 | -6 | -12 | 1 | -6 | -7 | -13 | -7 |
| R2008 | -21 | 19 | 0 | 9 | -9 | 0 | -12 | -20 |
| R2009 | -3 | 3 | -11 | 7 | 9 | -3 | -3 | -11 |
| R2010 | 10 | -2 | 7 | 2 | 1 | 19 | 9 | -4 |
| R2011 | 16 | 1 | -23 | 9 | -13 | 0 | 3 | -18 |
| R2012 | 21 | 22 | 32 | 13 | 6 | 31 | 23 | 20 |
| R2013 | 4 | 4 | 23 | -7 | 20 | 9 | -1 | 13 |
| R2014 | 24 | 27 | -3 | 6 | 4 | 0 | 14 | 23 |
| R2015 | 13 | 18 | 22 | 13 | 28 | 3 | -1 | -17 |
| R2017 | 11 | 5 | 2 | -14 | 0 | -3 | 2 | 6 |
| R2018 | -2 | -2 | -5 | -10 | 1 | 6 | 8 | 2 |
| R2019 | 8 | -8 | 3 | -2 | -18 | 0 | 2 | -4 |
| R2020 | 14 | 1 | 1 | -2 | 5 | -2 | 1 | 5 |
| Mean | 9.8 | 8.7 | 4.8 | 4.9 | 5.1 | 5.7 | 3.7 | 1.7 |
| Sum | 9.8 | 18.6 | 23.4 | 28.3 | 33.4 | 39.1 | 42.8 | 44.4 |

***TABLE 12A. (CONTINUED) CUMULATIVE SUM OF SYSTOLIC BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 26 | 4 | -4 | -27 |
| R2001 | 13 | 32 | 9 | 19 |
| R2002 | 24 | 14 | 6 | -3 |
| R2003 | -3 | 27 | 10 | 6 |
| R2004 | 18 | 15 | 7 | 19 |
| R2005 | 0 | 12 | -19 | |
| R2006 | 17 | 1 | 3 | -5 |
| R2007 | | | | |
| R2008 | -16 | -23 | 0 | -5 |
| R2009 | 4 | 4 | 12 | 1 |
| R2010 | -4 | -19 | 0 | 8 |
| R2011 | 0 | -13 | -19 | -5 |
| R2012 | 2 | 23 | 8 | -7 |
| R2013 | 23 | 5 | 17 | 11 |
| R2014 | 5 | | | |
| R2015 | -13 | 15 | 3 | 8 |
| R2017 | 12 | 22 | 33 | 9 |
| R2018 | -12 | 4 | 2 | -28 |
| R2019 | 8 | -7 | -16 | 4 |
| R2020 | 5 | -3 | -5 | -14 |
| Mean | 5.7 | 6.2 | 2.5 | -0.5 |
| Sum | 50.2 | 56.4 | 58.9 | 58.4 |

***TABLE 12B. CUMULATIVE SUM OF DIASTOLIC BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 10 | 10 | 11 | 23 | 21 | 21 | 19 | 15 |
| R2001 | 4 | 1 | 23 | 5 | -12 | -8 | 13 | -3 |
| R2002 | 2 | 19 | -7 | 5 | 7 | 10 | 6 | 17 |
| R2003 | 0 | -16 | -7 | 5 | 12 | 0 | 3 | -4 |
| R2004 | 5 | 8 | 4 | 1 | 7 | -1 | -1 | -4 |
| R2005 | 4 | 6 | 8 | 10 | 37 | 23 | 30 | 16 |
| R2006 | -5 | -11 | -7 | 4 | 5 | -8 | 3 | -5 |
| R2007 | 0 | -4 | -5 | -6 | -13 | -7 | -4 | -2 |
| R2008 | -7 | 9 | -4 | -6 | -16 | -10 | -12 | -2 |
| R2009 | -6 | -1 | -11 | 1 | 5 | -7 | 2 | -10 |
| R2010 | 4 | 8 | 17 | 3 | 10 | 10 | 0 | -4 |
| R2011 | 4 | 8 | 9 | 3 | 16 | 16 | 3 | 2 |
| R2012 | 4 | 8 | 3 | 3 | -6 | 6 | 16 | 13 |
| R2013 | 12 | 2 | 4 | 2 | 17 | 8 | 0 | 13 |
| R2014 | 12 | 1 | -2 | 0 | 1 | -2 | 10 | 1 |
| R2015 | -3 | 9 | 11 | 3 | 5 | 0 | 6 | -8 |
| R2017 | 5 | 3 | 1 | 12 | 4 | 7 | -4 | 1 |
| R2018 | -8 | 12 | 8 | 0 | 9 | 4 | 1 | 4 |
| R2019 | 5 | 4 | 8 | -11 | -6 | -12 | -2 | -1 |
| R2020 | 4 | 7 | 1 | -4 | 1 | -3 | 4 | -2 |
| Mean | 2.4 | 4.1 | 3.3 | 2.7 | 5.2 | 2.5 | 4.6 | 1.7 |
| Sum | 2.4 | 6.5 | 9.8 | 12.5 | 17.7 | 20.2 | 24.8 | 26.6 |

***TABLE 12B. (CONTINUED) CUMULATIVE SUM OF DIASTOLIC BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 23 | 13 | -17 | -17 |
| R2001 | 7 | 24 | 2 | 10 |
| R2002 | 18 | 10 | 7 | -1 |
| R2003 | 1 | 2 | 7 | -5 |
| R2004 | 15 | 10 | 16 | 16 |
| R2005 | -3 | 6 | -10 | |
| R2006 | 11 | -5 | -3 | -1 |
| R2007 | | | | |
| R2008 | -7 | -15 | 3 | -6 |
| R2009 | 2 | 2 | 4 | 1 |
| R2010 | 1 | -19 | 6 | 15 |
| R2011 | 14 | 11 | -9 | 6 |
| R2012 | -8 | 11 | 2 | -14 |
| R2013 | 18 | 5 | -2 | 6 |
| R2014 | -13 | | | |
| R2015 | -6 | 3 | -5 | 18 |
| R2017 | 6 | 31 | 21 | 17 |
| R2018 | -4 | 12 | 5 | -10 |
| R2019 | -10 | -8 | -16 | 2 |
| R2020 | -3 | -6 | -16 | -13 |
| Mean | 3.3 | 4.9 | -0.2 | 1.3 |
| Sum | 29.8 | 34.7 | 34.5 | 35.8 |

***TABLE 13A. CUMULATIVE SUM OF SYSTOLIC BLOOD PRESSURE REDUCTION FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | 8 | 13 | 19 | 12 | -6 | -22 | -8 | -5 |
| R2001 | -10 | 7 | 3 | -7 | 12 | 9 | 12 | -5 |
| R2002 | 15 | 11 | 4 | 7 | 8 | 6 | 13 | -1 |
| R2003 | 1 | 1 | -11 | 3 | 15 | 21 | 9 | 4 |
| R2004 | 13 | 8 | -11 | -6 | -11 | -9 | 4 | -17 |
| R2005 | 28 | 25 | 37 | 28 | 21 | -3 | -9 | -3 |
| R2006 | 4 | 2 | 2 | 9 | -3 | 3 | -9 | -10 |
| R2007 | 26 | 7 | 3 | 3 | 18 | 10 | 1 | 12 |
| R2008 | -10 | 10 | 7 | 16 | -17 | -14 | -20 | -12 |
| R2009 | 8 | 7 | 5 | -2 | 3 | -2 | -3 | -13 |
| R2010 | 13 | 14 | 0 | -6 | 11 | 30 | 4 | -7 |
| R2011 | 1 | 17 | -10 | 7 | -3 | -7 | -3 | -1 |
| R2012 | 11 | 29 | 33 | 29 | 11 | 14 | 8 | 13 |
| R2013 | 2 | 0 | 19 | -5 | 7 | -11 | -1 | -1 |
| R2014 | 18 | 27 | 0 | 0 | -13 | 7 | 19 | 15 |
| R2015 | 22 | 36 | 27 | 15 | 27 | 5 | 11 | 19 |
| R2017 | 9 | -15 | -1 | 5 | 0 | 5 | 5 | 16 |
| R2018 | 19 | -4 | -8 | 0 | 6 | 6 | -5 | -8 |
| R2019 | 9 | 4 | 7 | 11 | -6 | 7 | -10 | -1 |
| R2020 | 16 | -4 | 7 | -4 | -5 | -13 | -4 | 2 |
| Mean | 10.3 | 9.7 | 6.6 | 5.8 | 3.7 | 2.1 | 0.8 | -0.1 |
| Sum | 10.3 | 20.0 | 26.6 | 32.4 | 36.1 | 38.2 | 39.1 | 39.0 |

***TABLE 13A. (CONTINUED) CUMULATIVE SUM OF SYSTOLIC BLOOD PRESSURE REDUCTION FOLLOWING A CONTINUOUS PHYSICAL TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 23 | 3 | 12 | 10 |
| R2001 | 18 | 13 | -2 | 21 |
| R2002 | -5 | -13 | -8 | -13 |
| R2003 | -18 | -2 | -1 | 26 |
| R2004 | -24 | -11 | -24 | -2 |
| R2005 | -22 | -21 | -39 | -12 |
| R2006 | -6 | -3 | -20 | -11 |
| R2007 | | | | |
| R2008 | -14 | -15 | -21 | -24 |
| R2009 | 0 | 8 | 18 | -3 |
| R2010 | -3 | -12 | -7 | -15 |
| R2011 | 5 | -15 | -10 | -1 |
| R2012 | 13 | 12 | -3 | 1 |
| R2013 | 14 | -6 | 3 | 1 |
| R2014 | 3 | 20 | 25 | 22 |
| R2015 | 16 | 14 | 17 | -6 |
| R2017 | 26 | 22 | 27 | 2 |
| R2018 | 10 | 18 | 17 | -12 |
| R2019 | -3 | -7 | -17 | -4 |
| R2020 | 3 | 4 | -8 | 1 |
| Mean | 1.9 | 0.5 | -2.1 | -1.0 |
| Sum | 40.9 | 41.4 | 39.3 | 38.3 |

***TABLE 13B. CUMULATIVE SUM OF DIASTOLIC BLOOD PRESSURE REDUCTION FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **1 hour** | **2 hour** | **3 hour** | **4 hour** | **5 hour** | **6 hour** | **7 hour** | **8 hour** |
| R2000 | -1 | -2 | 11 | 22 | 19 | 20 | 15 | -1 |
| R2001 | 15 | 24 | 19 | 5 | 6 | -8 | 9 | 3 |
| R2002 | 9 | 14 | 4 | 4 | 9 | 10 | 4 | 6 |
| R2003 | -3 | -14 | -14 | -2 | 15 | -3 | 2 | -3 |
| R2004 | -2 | 17 | 3 | -2 | -4 | -8 | 9 | -4 |
| R2005 | 6 | 13 | 22 | 17 | 8 | 2 | 3 | 2 |
| R2006 | -8 | -7 | -4 | 4 | 4 | -3 | -11 | -9 |
| R2007 | 8 | 7 | 7 | -6 | 11 | 8 | 2 | 5 |
| R2008 | -5 | 2 | -8 | 0 | -11 | -17 | -12 | -2 |
| R2009 | 2 | 0 | 4 | -6 | 7 | 6 | 11 | -1 |
| R2010 | 6 | 5 | 7 | 13 | 10 | 6 | -2 | -5 |
| R2011 | 10 | -2 | -1 | 13 | 21 | 16 | 0 | 7 |
| R2012 | -1 | 6 | 5 | 8 | 2 | -1 | 6 | 8 |
| R2013 | 5 | -10 | -1 | -3 | -1 | -5 | 4 | -7 |
| R2014 | 14 | 8 | 0 | 2 | -13 | 0 | 9 | 1 |
| R2015 | 6 | 15 | 20 | 4 | 7 | 1 | 9 | 4 |
| R2017 | -7 | -7 | -11 | 0 | 2 | -3 | 0 | 6 |
| R2018 | 3 | 1 | -5 | -1 | 11 | 0 | -3 | 6 |
| R2019 | 7 | 7 | 12 | -1 | 1 | -3 | 0 | 1 |
| R2020 | -6 | -7 | -8 | 6 | -14 | -13 | 17 | -2 |
| Mean | 2.9 | 3.5 | 3.1 | 3.7 | 4.5 | 0.3 | 3.6 | 0.7 |
| Sum | 2.9 | 6.3 | 9.4 | 13.1 | 17.7 | 18.0 | 21.5 | 22.2 |

***TABLE 13B. (CONTINUED) CUMULATIVE SUM OF DIASTOLIC BLOOD PRESSURE REDUCTION FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Hourly Mean Blood Pressure Reduction (mm Hg) Following a Treatment*** | | | |
|---|---|---|---|---|
| **ID** | **9 hour** | **10 hour** | **11 hour** | **12 hour** |
| R2000 | 15 | 18 | -9 | 12 |
| R2001 | 26 | 10 | 1 | 21 |
| R2002 | -1 | -10 | -6 | -11 |
| R2003 | -5 | -13 | -3 | 19 |
| R2004 | 0 | 0 | -6 | -5 |
| R2005 | -20 | -26 | -21 | -9 |
| R2006 | -3 | -3 | -16 | -2 |
| R2007 | | | | |
| R2008 | -3 | -5 | -10 | -17 |
| R2009 | 4 | 4 | 14 | 0 |
| R2010 | -9 | -19 | 4 | 1 |
| R2011 | 18 | 7 | -18 | 3 |
| R2012 | -3 | -4 | -12 | -9 |
| R2013 | 4 | -9 | -6 | -7 |
| R2014 | -14 | -4 | -5 | -2 |
| R2015 | 5 | 7 | 6 | 2 |
| R2017 | 24 | 29 | 29 | 10 |
| R2018 | -3 | 11 | 8 | 3 |
| R2019 | -10 | -3 | -17 | -4 |
| R2020 | -3 | -6 | -11 | -4 |
| Mean | 1.2 | -0.8 | -3.9 | 0.1 |
| Sum | 23.5 | 22.7 | 18.8 | 18.9 |

***TABLE 14. MAGNITUDE OF BLOOD PRESSURE REDUCTION FOR THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | *Systolic Blood Pressure (mm Hg)* | | |
|---|---|---|---|
| **ID** | **CONTROL** | **ACCUMULATION** | **DIFFERENCE** |
| R2000 | 144.2 | 139.1 | 5.1 |
| R2001 | 131.5 | 120.2 | 11.3 |
| R2002 | 132.1 | 118.5 | 13.6 |
| R2003 | 128.0 | 121.2 | 6.8 |
| R2004 | 111.0 | 103.1 | 7.8 |
| R2005 | 137.4 | 119.5 | 17.9 |
| R2006 | 123.6 | 117.5 | 6.1 |
| R2007 | 129.9 | 136.7 | -6.8 |
| R2008 | 122.0 | 128.6 | -6.7 |
| R2009 | 148.3 | 147.5 | 0.8 |
| R2010 | 132.4 | 130.8 | 1.6 |
| R2011 | 127.7 | 132.8 | -5.2 |
| R2012 | 138.2 | 119.9 | 18.3 |
| R2013 | 133.7 | 123.7 | 10.1 |
| R2014 | 136.5 | 122.9 | 13.7 |
| R2015 | 137.5 | 129.7 | 7.8 |
| R2017 | 138.2 | 131.3 | 6.9 |
| R2018 | 133.3 | 134.1 | -0.8 |
| R2019 | 123.8 | 126.9 | -3.2 |
| R2020 | 137.0 | 135.1 | 1.9 |
| Mean | 132.1 | 126.5 | 5.5 |
| SD | 8.33 | 9.73 | 7.60 |
| SE | 1.86 | 2.18 | 1.70 |

Systolic blood pressures represent 11-hour average values.

***TABLE 14. (CONTINUED) MAGNITUDE OF BLOOD PRESSURE REDUCTION FOR THE ACCUMULATION OF PHYSICAL ACTIVITY TREATMENT***

| | ***Diastolic Blood Pressure (mm Hg)*** | | |
|---|---|---|---|
| **ID** | **CONTROL** | **ACCUMULATION** | **DIFFERENCE** |
| R2000 | 98.1 | 81.5 | 16.56 |
| R2001 | 80.9 | 75.5 | 5.46 |
| R2002 | 87.7 | 79.2 | 8.54 |
| R2003 | 84.7 | 85.1 | -0.41 |
| R2004 | 63.4 | 58.9 | 4.52 |
| R2005 | 76.6 | 62.9 | 13.64 |
| R2006 | 71.6 | 73.3 | -1.69 |
| R2007 | 87.1 | 91.5 | -4.39 |
| R2008 | 69.4 | 76.4 | -6.95 |
| R2009 | 94.1 | 96.4 | -2.33 |
| R2010 | 82.1 | 79.1 | 2.99 |
| R2011 | 87.2 | 78.8 | 8.45 |
| R2012 | 83.2 | 78.1 | 5.11 |
| R2013 | 83.5 | 75.3 | 8.15 |
| R2014 | 80.3 | 79.9 | 0.42 |
| R2015 | 75.7 | 73.7 | 1.99 |
| R2017 | 75.6 | 71.7 | 3.86 |
| R2018 | 71.7 | 75.1 | -3.38 |
| R2019 | 82.4 | 82.6 | -0.24 |
| R2020 | 82.8 | 76.0 | 6.82 |
| Mean | 80.80 | 77.63 | 3.17 |
| SD | 8.31 | 8.30 | 6.00 |
| SE | 1.86 | 1.86 | 1.34 |

Diastolic blood pressures represent 10-hour average values.

***TABLE 15. MAGNITUDE OF BLOOD PRESSURE REDUCTION FOR A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Systolic Blood Pressure (mm Hg)*** | | |
|---|---|---|---|
| **ID** | **CONTROL** | **CONTINUOUS** | **DIFFERENCE** |
| R2000 | 139.7 | 137.5 | 2.3 |
| R2001 | 135.8 | 132.3 | 3.6 |
| R2002 | 136.5 | 127.5 | 9.0 |
| R2003 | 129.3 | 123.5 | 5.7 |
| R2004 | 111.3 | 112.9 | -1.6 |
| R2005 | 153.0 | 134.8 | 18.2 |
| R2006 | 126.3 | 124.9 | 1.4 |
| R2007 | 129.4 | 119.6 | 9.8 |
| R2008 | 128.3 | 132.4 | -4.1 |
| R2009 | 147.5 | 145.3 | 2.2 |
| R2010 | 135.7 | 126.3 | 9.3 |
| R2011 | 131.5 | 131.1 | 0.3 |
| R2012 | 144.6 | 125.2 | 19.4 |
| R2013 | 132.6 | 130.8 | 1.8 |
| R2014 | 130.8 | 122.4 | 8.4 |
| R2015 | 139.3 | 118.9 | 20.4 |
| R2017 | 137.2 | 136.0 | 1.3 |
| R2018 | 130.5 | 128.4 | 2.1 |
| R2019 | 124.8 | 121.7 | 3.1 |
| R2020 | 139.0 | 140.0 | -0.9 |
| Mean | 133.9 | 128.0 | 5.9 |
| SD | 8.33 | 9.73 | 7.60 |
| SE | 1.86 | 2.18 | 1.70 |

Systolic blood pressures represent 7-hour average values.

***TABLE 15. (CONTINUED) MAGNITUDE OF BLOOD PRESSURE REDUCTION FOR A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Diastolic Blood Pressure (mm Hg)*** | | |
|---|---|---|---|
| **ID** | **CONTROL** | **CONTINUOUS** | **DIFFERENCE** |
| R2000 | 98.1 | 86.3 | 11.9 |
| R2001 | 85.0 | 75.1 | 9.9 |
| R2002 | 89.6 | 81.9 | 7.7 |
| R2003 | 85.8 | 88.3 | -2.5 |
| R2004 | 62.8 | 60.9 | 1.9 |
| R2005 | 82.0 | 72.1 | 9.8 |
| R2006 | 71.1 | 74.8 | -3.7 |
| R2007 | 86.5 | 81.4 | 5.1 |
| R2008 | 71.3 | 78.6 | -7.3 |
| R2009 | 93.8 | 90.3 | 3.5 |
| R2010 | 84.9 | 78.5 | 6.4 |
| R2011 | 88.9 | 80.8 | 8.1 |
| R2012 | 85.1 | 81.6 | 3.5 |
| R2013 | 82.8 | 84.2 | -1.4 |
| R2014 | 81.2 | 78.3 | 2.9 |
| R2015 | 76.7 | 67.9 | 8.8 |
| R2017 | 74.9 | 74.0 | 0.9 |
| R2018 | 73.1 | 69.8 | 3.2 |
| R2019 | 82.4 | 85.8 | -3.5 |
| R2020 | 82.0 | 85.6 | -3.6 |
| Mean | 81.9 | 78.5 | 3.4 |
| SD | 8.36 | 7.43 | 5.44 |
| SE | 1.87 | 1.66 | 1.22 |

Diastolic blood pressures represent 7-hour average values.

***TABLE 16. AREAS OF BLOOD PRESSURE REDUCTION FOLLOWING PHYSICAL ACTIVITY TREATMENTS***

| | ***Area of SBP Reduction (mm Hg·hour)*** | | ***Area of DBP Reduction (mm Hg·hour)*** | |
|---|---|---|---|---|
| **ID** | **ACCUMULATION** | **CONTINUOUS** | **ACCUMULATION** | **CONTINUOUS** |
| C2000 | 35.4 | 3.5 | 155.7 | 73.5 |
| C2001 | 119.8 | 14.4 | 51.3 | 59.2 |
| C2002 | 146.8 | 64.7 | 85.8 | 57.9 |
| C2003 | 61.7 | 19.3 | -0.2 | -14.0 |
| C2004 | 75.2 | -14.5 | 48.1 | 16.8 |
| C2005 | 203.7 | 127.2 | 137.3 | 71.4 |
| C2006 | 61.2 | 5.5 | -14.5 | -25.1 |
| C2007 | 95.2 | 69.4 | -31.1 | 39.0 |
| C2008 | -77.4 | -21.8 | -78.5 | -53.3 |
| C2009 | -8.2 | 11.9 | -26.0 | 19.6 |
| C2010 | 28.7 | 62.5 | 41.7 | 41.8 |
| C2011 | -0.3 | -30.8 | 90.4 | 40.1 |
| C2012 | 173.2 | 139.9 | 19.4 | 25.9 |
| C2013 | 95.3 | 4.2 | 78.7 | -10.5 |
| C2014 | 455.4 | 50.8 | 123.1 | 15.9 |
| C2015 | 78.3 | 128.2 | 20.3 | 56.1 |
| C2017 | 73.3 | 4.2 | 65.1 | -30.1 |
| C2018 | 0.3 | 10.7 | 43.3 | 6.4 |
| C2019 | -38.5 | 13.6 | -35.0 | 18.8 |
| C2020 | 19.3 | -6.1 | -2.1 | -29.2 |
| Mean | 79.91 | 32.83 | 38.63 | 19.00 |
| SD | 112.36 | 50.72 | 61.97 | 36.75 |
| SE | 25.12 | 11.34 | 13.86 | 8.22 |

SBP = systolic blood pressure, DBP = diastolic blood pressure

Areas of systolic blood pressure reduction for the accumulation of short bouts and a long bout of exercise treatments were 11-hour and 7 hour averages, respectively. Areas of diastolic blood pressure reduction for the accumulation of short bouts and a long bout of exercise treatments were 10-hour and 7 hour averages, respectively.

***TABLE 17. ENERGY EXPENDITURE FOLLOWING PHYSICAL ACTIVITY TREATMENTS***

| | ***Energy Expenditure for 12 hours (kcal)*** | | |
|---|---|---|---|
| **ID** | **CONTROL** | **ACCUMULATION** | **CONTINUOUS** |
| R2000 | 355.6 | | 264.7 |
| R2001 | 320.4 | 340.3 | 416.8 |
| R2002 | 391.6 | 228.2 | 182.7 |
| R2003 | | | |
| R2004 | 110.5 | 130.8 | 182.4 |
| R2005 | 328.7 | 343.1 | 263.6 |
| R2006 | 483.0 | 317.6 | 332.7 |
| R2007 | 730.3 | 301.3 | 546.4 |
| R2008 | 344.9 | 194.6 | 243.4 |
| R2009 | 255.6 | 290.4 | 324.4 |
| R2010 | 517.9 | 365.3 | 312.1 |
| R2011 | 450.0 | 460.6 | 208.1 |
| R2012 | 163.8 | 248.5 | 325.1 |
| R2013 | 260.5 | 315.9 | 210.2 |
| R2014 | 226.2 | 438.5 | 222.6 |
| R2015 | 153.3 | 231.0 | 319.2 |
| R2017 | 307.3 | 561.3 | 570.8 |
| R2018 | 517.8 | 569.7 | 716.4 |
| R2019 | | | |
| R2020 | 407.6 | 587.9 | 320.4 |
| Mean | 351.39 | 348.51 | 331.22 |
| SD | 153.37 | 134.53 | 146.06 |
| SE | 34.29 | 30.08 | 32.66 |

***TABLE 18. AVERAGE HEART RATE VARIABILITY FOLLOWING A CONTROL TREATMENT***

| | ***Normalized Low Frequency Power (%)*** | | | ***Normalized High Frequency Power (%)*** | | | ***Low to High Frequency Power Ratio*** | | |
|---|---|---|---|---|---|---|---|---|---|
| **ID** | **7 hour** | **10 hour** | **11 hour** | **7 hour** | **10 hour** | **11 hour** | **7 hour** | **10 hour** | **11 hour** |
| R2000 | 86.67 | 84.89 | 83.73 | 12.23 | 13.90 | 14.91 | 7.57 | 6.67 | 6.33 |
| R2001 | 84.76 | 83.96 | 84.27 | 13.84 | 14.04 | 13.83 | 6.52 | 6.39 | 6.48 |
| R2002 | 73.39 | 68.75 | 65.46 | 21.24 | 26.79 | 30.35 | 3.64 | 3.10 | 2.87 |
| R2003 | 81.87 | 82.28 | 82.63 | 16.54 | 16.25 | 15.95 | 6.00 | 5.95 | 6.01 |
| R2004 | 53.79 | 63.15 | 63.61 | 38.45 | 31.15 | 31.04 | 2.20 | 3.50 | 3.39 |
| R2005 | 73.45 | 69.03 | 66.23 | 22.58 | 26.27 | 28.53 | 4.15 | 3.51 | 3.26 |
| R2006 | 66.90 | 68.73 | 69.29 | 28.43 | 27.06 | 26.64 | 2.46 | 2.69 | 2.74 |
| R2007 | 69.15 | 71.08 | 71.92 | 23.55 | 23.03 | 22.60 | 3.69 | 3.65 | 3.72 |
| R2008 | 72.88 | 65.12 | 65.12 | 23.52 | 31.75 | 31.84 | 3.30 | 2.60 | 2.55 |
| R2009 | | | | | | | | | |
| R2010 | 67.14 | 66.32 | 65.54 | 29.50 | 30.87 | 31.71 | 2.70 | 2.50 | 2.40 |
| R2011 | 85.97 | 81.81 | 81.39 | 10.78 | 14.38 | 14.81 | 8.48 | 7.03 | 6.76 |
| R2012 | 69.51 | 65.06 | 62.58 | 26.86 | 31.13 | 33.59 | 3.31 | 2.90 | 2.70 |
| R2013 | | | | | | | | | |
| R2014 | 80.41 | 79.63 | 79.96 | 18.05 | 18.86 | 18.61 | 5.27 | 4.87 | 4.90 |
| R2015 | 68.20 | 69.16 | 67.50 | 27.56 | 26.60 | 28.23 | 2.56 | 2.68 | 2.54 |
| R2017 | 87.09 | 86.65 | 86.65 | 12.05 | 12.44 | 12.45 | 7.38 | 7.14 | 7.11 |
| R2018 | 76.74 | 76.24 | 76.56 | 20.69 | 21.21 | 20.93 | 4.13 | 3.94 | 3.98 |
| R2019 | 83.36 | 81.21 | 78.02 | 14.45 | 16.50 | 19.65 | 6.05 | 5.32 | 4.92 |
| R2020 | 79.91 | 77.88 | 77.51 | 18.29 | 20.45 | 20.89 | 4.51 | 4.27 | 4.15 |
| Mean | 75.62 | 74.50 | 73.78 | 21.03 | 22.37 | 23.14 | 4.66 | 4.37 | 4.27 |
| SD | 8.95 | 7.87 | 8.22 | 7.34 | 6.78 | 7.16 | 1.93 | 1.65 | 1.64 |
| SE | 2.11 | 1.86 | 1.94 | 1.73 | 1.60 | 1.69 | 0.46 | 0.39 | 0.39 |

***TABLE 19. AVERAGE HEART RATE VARIABILITY FOLLOWING THE ACCUMULATION OF PHYSICAL ACTIVITY***

***TREATMENT***

| | ***Normalized Low Frequency Power (%)*** | | ***Normalized High Frequency Power (%)*** | | ***Low to High Frequency Power Ratio*** | |
|---|---|---|---|---|---|---|
| **ID** | **10 hour** | **11 hour** | **10 hour** | **11 hour** | **10 hour** | **11 hour** |
| R2000 | 76.89 | 75.84 | 18.70 | 19.74 | 4.57 | 4.35 |
| R2001 | 84.09 | 83.24 | 13.93 | 14.82 | 6.34 | 6.05 |
| R2002 | 62.03 | 59.74 | 34.97 | 37.39 | 2.50 | 2.33 |
| R2003 | 88.06 | 88.11 | 10.86 | 10.86 | 8.90 | 8.84 |
| R2004 | 69.71 | 70.38 | 28.13 | 27.33 | 3.11 | 3.20 |
| R2005 | 40.43 | 41.75 | 47.75 | 46.81 | 0.95 | 1.00 |
| R2006 | 74.52 | 73.48 | 22.03 | 22.88 | 3.49 | 3.35 |
| R2007 | 81.76 | 79.13 | 14.65 | 17.40 | 7.28 | 6.73 |
| R2008 | 73.72 | 73.44 | 23.15 | 23.39 | 3.58 | 3.50 |
| R2009 | | | | | | |
| R2010 | 72.85 | 73.08 | 24.28 | 24.08 | 3.44 | 3.44 |
| R2011 | 82.50 | 81.23 | 13.54 | 14.74 | 6.55 | 6.18 |
| R2012 | 63.80 | 63.20 | 30.05 | 30.85 | 2.84 | 2.71 |
| R2013 | | | | | | |
| R2014 | 83.44 | 82.34 | 14.68 | 15.81 | 7.54 | 7.09 |
| R2015 | 69.08 | 69.03 | 27.31 | 27.44 | 2.63 | 2.60 |
| R2017 | 88.20 | 87.44 | 10.76 | 11.50 | 8.86 | 8.44 |
| R2018 | 76.16 | 75.49 | 21.60 | 22.25 | 3.93 | 3.79 |
| R2019 | 84.83 | 83.53 | 13.85 | 14.97 | 6.30 | 5.97 |
| R2020 | 75.92 | 75.35 | 22.76 | 23.35 | 4.67 | 4.47 |
| Mean | 74.89 | 74.21 | 21.83 | 22.53 | 4.86 | 4.67 |
| SD | 11.53 | 11.14 | 9.52 | 9.22 | 2.33 | 2.20 |
| SE | 2.72 | 2.63 | 2.24 | 2.17 | 0.55 | 0.52 |

***TABLE 20. AVERAGE HEART RATE VARIABILITY FOLLOWING A CONTINUOUS PHYSICAL ACTIVITY TREATMENT***

| | ***Normalized Low Frequency Power (%)*** | ***Normalized High Frequency Power (%)*** | ***Low to High Frequency Power Ratio*** |
|---|---|---|---|
| **ID** | **7 hour** | **7 hour** | **7 hour** |
| R2000 | 82.37 | 15.12 | 5.87 |
| R2001 | 80.55 | 17.75 | 4.81 |
| R2002 | 76.21 | 21.10 | 3.85 |
| R2003 | 89.83 | 9.01 | 11.07 |
| R2004 | 78.14 | 19.37 | 4.84 |
| R2005 | 43.95 | 43.29 | 1.17 |
| R2006 | 74.25 | 21.65 | 3.61 |
| R2007 | 71.23 | 21.22 | 3.78 |
| R2008 | 70.17 | 26.46 | 2.95 |
| R2009 | | | |
| R2010 | 72.32 | 25.85 | 3.07 |
| R2011 | 83.53 | 11.80 | 7.71 |
| R2012 | 76.80 | 18.64 | 4.35 |
| R2013 | | | |
| R2014 | 81.86 | 16.04 | 5.51 |
| R2015 | 64.37 | 28.89 | 2.30 |
| R2017 | 89.27 | 9.99 | 9.30 |
| R2018 | 86.22 | 11.78 | 7.95 |
| R2019 | 81.93 | 16.15 | 5.32 |
| R2020 | 77.32 | 21.02 | 3.84 |
| Mean | 76.68 | 19.73 | 5.07 |
| SD | 10.55 | 8.12 | 2.53 |
| SE | 2.49 | 1.91 | 0.60 |

***TABLE 21A. NORMALIZED LOW FREQUENCY POWER OF HEART RATE VARIABILITY FOR BASELINE AND FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

| | ***Normalized Low Frequency Power (%)*** | | | | | | |
|---|---|---|---|---|---|---|---|
| **ID** | **Baseline** | | **1st** | | **2nd** | | **3rd** |
| R2000 | 78.037 | | 88.995 | | 88.165 | | 88.594 |
| R2001 | 82.552 | | 84.691 | | 86.38 | | 87.586 |
| R2002 | 82.765 | | 83.687 | | 84.093 | | 91.038 |
| R2003 | 75.153 | | 76.92 | | 94.401 | | 86.913 |
| R2004 | 68.838 | | 68.028 | | 69.752 | | 52.44 |
| R2005 | 74.563 | | 69.109 | | 61.476 | | 47.089 |
| R2007 | 68.459 | | 76.644 | | 73.454 | | 88.655 |
| R2008 | 83.197 | | 80.589 | | 80.161 | | 48.063 |
| R2009 | 79.787 | | 86.263 | | 91.143 | | 92.224 |
| R2010 | 80.814 | | 53.402 | | 78.119 | | 79.008 |
| R2011 | 81.525 | | 87.198 | | 83.001 | | 87.132 |
| R2012 | 85.073 | | 62.215 | | 48.283 | | 62.852 |
| R2013 | 85.377 | | 81.368 | | 87.072 | | 83.65 |
| R2014 | 90.812 | | 88.632 | | 88.848 | | 88.61 |
| R2015 | 71.533 | | 76.459 | | 79.341 | | 80.13 |
| R2016 | 76.844 | | 79.782 | | 64.463 | | 60.132 |
| R2017 | 87.179 | | 87.407 | | 85.092 | | 83.47 |
| R2018 | 81.247 | | 93.228 | | 89.857 | | 93.641 |
| R2019 | 83.323 | | 90.667 | | 87.63 | | 85.544 |
| R2020 | 82.188 | | 85.96 | | 81.431 | | 84.842 |
| Mean | 79.96 | | 80.06 | | 80.11 | | 78.58 |
| SD | 5.91 | | 10.21 | | 11.51 | | 15.27 |
| SE | 1.32 | | 2.28 | | 2.57 | | 3.41 |

Values of heart rate variability were average for 15-minute baseline and the last 40 minutes of rest period following successive short sessions of exercise treatment.

***Table 21b. NORMALIZED HIGH FREQUENCY POWER OF HEART RATE VARIABILITY FOR BASELINE AND FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

| | ***Normalized High Frequency Power (%)*** | | | | | | |
|---|---|---|---|---|---|---|---|
| **ID** | **Baseline** | | **1st** | | **2nd** | | **3rd** |
| R2000 | 20.694 | | | | 11.148 | | 10.785 |
| R2001 | 15.985 | | 14.044 | | 12.262 | | 11.047 |
| R2002 | 15.676 | | 14.721 | | 13.71 | | 7.633 |
| R2003 | 22.601 | | 20.861 | | 5.196 | | 12.02 |
| R2004 | 28.634 | | 28.964 | | 25.804 | | 44.781 |
| R2005 | 20.364 | | 24.498 | | 30.959 | | 43.432 |
| R2006 | | | | | | | |
| R2007 | 27.135 | | 20.274 | | 21.755 | | 8.365 |
| R2008 | 15.447 | | 17.496 | | 18.212 | | 45.507 |
| R2009 | 16.828 | | 11.069 | | 7.029 | | 6.247 |
| R2010 | 17.634 | | 44.764 | | 20.693 | | 19.763 |
| R2011 | 16.342 | | 11.566 | | 14.429 | | 10.883 |
| R2012 | 13.019 | | 29.947 | | 47.356 | | 32.981 |
| R2013 | 13.599 | | 17.534 | | 12.452 | | 14.385 |
| R2014 | 8.632 | | 8.867 | | 9.635 | | 9.452 |
| R2015 | 24.037 | | 22.01 | | 18.963 | | 18.269 |
| R2016 | 22.045 | | 19.265 | | 34.356 | | 38.559 |
| R2017 | 11.936 | | 11.822 | | 14.24 | | 15.646 |
| R2018 | 17.168 | | 5.656 | | 9.176 | | 5.349 |
| R2019 | 15.077 | | 8.392 | | 11.375 | | 13.516 |
| R2020 | 15.876 | | 12.985 | | 17.227 | | 14.173 |
| Mean | 17.94 | | 18.14 | | 17.80 | | 19.14 |
| S.D. | 5.06 | | 9.31 | | 10.29 | | 13.68 |
| S.E. | 1.13 | | 2.08 | | 2.30 | | 3.06 |

Values of heart rate variability were average for 15-minute baseline and the last 40 minutes of rest period following successive short sessions of exercise treatment.

***Table 21c. LOW TO HIGH FREQUENCY POWER OF HEART RATE VARIABILITY FOR BASELINE AND FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

| | ***Normalized High Frequency Power (%)*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **ID** | **Baseline** | | **1st** | | **2nd** | | **3rd** | |
| R2000 | 3.771 | | 8.575 | | 7.908 | | 8.214 | |
| R2001 | 5.164 | | 6.03 | | 7.045 | | 7.929 | |
| R2002 | 5.28 | | 5.685 | | 6.134 | | 11.927 | |
| R2003 | 3.325 | | 3.687 | | 18.167 | | 7.231 | |
| R2004 | 2.404 | | 2.349 | | 2.703 | | 1.171 | |
| R2005 | 3.662 | | 2.821 | | 1.986 | | 1.084 | |
| R2006 | | | | | | | | |
| R2007 | 2.523 | | 3.78 | | 3.376 | | 10.599 | |
| R2008 | 5.386 | | 4.606 | | 4.402 | | 1.056 | |
| R2009 | 4.741 | | 7.793 | | 12.968 | | 14.764 | |
| R2010 | 4.583 | | 1.193 | | 3.775 | | 3.998 | |
| R2011 | 4.989 | | 7.539 | | 5.752 | | 8.006 | |
| R2012 | 6.534 | | 2.078 | | 1.02 | | 1.906 | |
| R2013 | 6.278 | | 4.641 | | 6.992 | | 5.815 | |
| R2014 | 10.521 | | 9.996 | | 9.221 | | 9.374 | |
| R2015 | 2.976 | | 3.474 | | 4.184 | | 4.386 | |
| R2016 | 3.486 | | 4.141 | | 1.876 | | 1.559 | |
| R2017 | 7.304 | | 7.394 | | 5.976 | | 5.335 | |
| R2018 | 4.732 | | 16.484 | | 9.793 | | 17.505 | |
| R2019 | 5.527 | | 10.805 | | 7.704 | | 6.329 | |
| R2020 | 5.177 | | 6.62 | | 4.727 | | 5.986 | |
| Mean | 4.92 | | 5.98 | | 6.29 | | 6.71 | |
| S.D. | 1.86 | | 3.62 | | 4.08 | | 4.57 | |
| S.E. | 0.42 | | 0.81 | | 0.91 | | 1.02 | |

Values of heart rate variability were average for 15-minute baseline and the last 40 minutes of rest period following successive short sessions of exercise treatment.

## *APPENDIX D - STATISTICAL SUMMARIES*

***TABLE 1. DEMOGRAPHICS OF SUBJECTS***

**Descriptive Statistics**

| | N | Minimum | Maximum | Mean | | Std. |
|---|---|---|---|---|---|---|
| | Statistic | Statistic | Statistic | Statistic | Std. Error | Statistic |
| Age | 20 | 25.00 | 66.00 | 47.1500 | 2.92113 | 13.06371 |
| Ht | 20 | 156.00 | 186.70 | 176.3150 | 1.70575 | 7.62836 |
| Wt | 20 | 46.40 | 138.10 | 84.4730 | 4.38527 | 19.61152 |
| BMI | 20 | 19.07 | 40.44 | 26.9965 | 1.16848 | 5.22559 |
| VO2 | 20 | 24.85 | 48.70 | 34.4763 | 1.63559 | 7.31458 |
| SBP | 20 | 123.00 | 139.70 | 131.8450 | 1.05440 | 4.71543 |
| DBP | 20 | 68.70 | 89.00 | 82.4500 | 1.41937 | 6.34761 |
| Valid N (listwise) | 20 | | | | | |

Age (years), Ht = height (cm), Wt = weight (kg), BMI = body mass index (kg/m2), $VO_2$ = peak oxygen uptake (kg/ml/min),

SBP = screening systolic blood pressure (mm Hg), DBP = screening diastolic blood pressure (mm Hg)

***TABLE 2. CORRELATIONS BETWEEN SYSTOLIC BLOOD PRESSURE REDUCTION AND CONFOUNDING VARIABLES***

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| SBP | 5.3555 | 7.58854 | 20 |
| AGE | 47.1500 | 13.06371 | 20 |
| BMI | 26.9965 | 5.22559 | 20 |
| energy expenditure | 342.9967 | 114.13919 | 18 |

Correlations

| | | SBP | AGE | BMI | energy expenditure |
|---|---|---|---|---|---|
| SBP | Pearson Correlation | 1 | -.215 | .405 | -.399 |
| | Sig. (2-tailed) | | .362 | .077 | .101 |
| | N | 20 | 20 | 20 | 18 |
| AGE | Pearson Correlation | -.215 | 1 | -.592(**) | -.263 |
| | Sig. (2-tailed) | .362 | | .006 | .292 |
| | N | 20 | 20 | 20 | 18 |
| BMI | Pearson Correlation | .405 | -.592(**) | 1 | .396 |
| | Sig. (2-tailed) | .077 | .006 | | .104 |
| | N | 20 | 20 | 20 | 18 |
| energy expenditure | Pearson Correlation | -.399 | -.263 | .396 | 1 |
| | Sig. (2-tailed) | .101 | .292 | .104 | |
| | N | 18 | 18 | 18 | 18 |

** Correlation is significant at the 0.01 level (2-tailed).

SBP = systolic blood pressure reduction (mm Hg), age (years), BMI = body mass index (kg/m2), energy expenditure (kcal)

***Table 3. MAGNITUDE OF BLOOD PRESSURE REDUCTION***

Paired Samples Statistics

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Pair 1 | 11 hr SBP | 132.3070 | 20 | 8.32604 | 1.86176 |
| | 11 hr SBP | 126.9525 | 20 | 9.72810 | 2.17527 |
| Pair 2 | 7hr SBP | 134.1485 | 20 | 8.97254 | 2.00632 |
| | 7hr SBP | 128.5670 | 20 | 7.88483 | 1.76310 |
| Pair 3 | 10 hr DBP | 80.9045 | 20 | 8.30844 | 1.85782 |
| | 10hr DBP | 77.5480 | 20 | 8.30038 | 1.85602 |
| Pair 4 | 7hr DBP | 81.8835 | 20 | 8.35694 | 1.86867 |
| | 7hr DBP | 78.8055 | 20 | 7.42662 | 1.66064 |

SBP = systolic blood pressure (mm Hg), DBP = diastolic blood pressure (mm Hg)

Pair 1 = 11-hour mean systolic blood pressures from a control and the accumulation of short bouts of exercise treatments

Pair 2 = 7-hour mean systolic blood pressures from a control and a long bout of exercise treatments

Pair 3 = 10-hour mean diastolic blood pressures from a control and the accumulation of short bouts of exercise treatments

Pair 4 = 7-hour mean diastolic blood pressures from a control and a long bout of exercise treatments

***TABLE 3. (CONTINUED) MAGNITUDE OF BLOOD PRESSURE REDUCTION***

Paired Samples Test

| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | | |
| | | | | | Lower | Upper | | | |
| Pair 1 | 11 hr SBP - 11 hr SBP | 5.35450 | 7.59062 | 1.69731 | 1.80198 | 8.90702 | 3.155 | 19 | .005 |
| Pair 2 | 7hr SBP - 7hr SBP | 5.58150 | 6.99658 | 1.56448 | 2.30700 | 8.85600 | 3.568 | 19 | .002 |
| Pair 3 | 10 hr DBP - 10hr DBP | 3.35650 | 6.00063 | 1.34178 | .54812 | 6.16488 | 2.502 | 19 | .022 |
| Pair 4 | 7hr DBP - 7hr DBP | 3.07800 | 5.44185 | 1.21683 | .53114 | 5.62486 | 2.530 | 19 | .020 |

SBP = systolic blood pressure (mm Hg), DBP = diastolic blood pressure (mm Hg)

Pair 1 = 11-hour mean systolic blood pressures from a control and the accumulation of short bouts of exercise treatments

Pair 2 = 7-hour mean systolic blood pressures from a control and a long bout of exercise treatments

Pair 3 = 10-hour mean diastolic blood pressures from a control and the accumulation of short bouts of exercise treatments

Pair 4 = 7-hour mean diastolic blood pressures from a control and a long bout of exercise treatments

***TABLE 4. AREAS OF BLOOD PRESSURE REDUCTION***

Paired Samples Statistics

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Pair 1 | SBP area - 11hr | 79.9090 | 20 | 112.35628 | 25.12363 |
| | SBP area - 7hr | 32.8340 | 20 | 50.71918 | 11.34115 |
| Pair 2 | DBP area - 10hr | 38.6295 | 20 | 61.96703 | 13.85625 |
| | DBP area - 7hr | 19.0005 | 20 | 36.75081 | 8.21773 |

Paired Samples Test

| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference Lower | Upper | | | |
| Pair 1 | SBP area - 11hr - SBP area - 7hr | 47.07500 | 98.23932 | 21.96698 | 1.09758 | 93.05242 | 2.143 | 19 | .045 |
| Pair 2 | DBP area - 10hr - DBP area - 7hr | 19.62900 | 51.55373 | 11.52777 | -4.49889 | 43.75689 | 1.703 | 19 | .105 |

SBP area = area of systolic blood pressure reduction (mm Hg•hr), DBP area = area of diastolic blood pressure reduction (mm Hg•hr)

***TABLE 5. AMBULATORY BLOOD PRESSURE MONITORING***

Within-Subjects Factors

Measure: MEASURE_1

| Factor1 | Dependent Variable |
|---|---|
| 1 | Control |
| 2 | Accumulation |
| 3 | Long |

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| Control | 93.8300 | 7.04722 | 20 |
| Accumulation | 92.1300 | 10.48071 | 20 |
| Long | 91.5350 | 8.05705 | 20 |

***TABLE 5. (CONTINUED) AMBULATORY BLOOD PRESSURE MONITORING***

Tests of Within-Subjects Effects

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 56.740 | 2 | 28.370 | .903 | .414 |
| | Greenhouse-Geisser | 56.740 | 1.605 | 35.348 | .903 | .396 |
| | Huynh-Feldt | 56.740 | 1.731 | 32.786 | .903 | .402 |
| | Lower-bound | 56.740 | 1.000 | 56.740 | .903 | .354 |
| Error(factor1) | Sphericity Assumed | 1193.906 | 38 | 31.419 | | |
| | Greenhouse-Geisser | 1193.906 | 30.498 | 39.146 | | |
| | Huynh-Feldt | 1193.906 | 32.882 | 36.309 | | |
| | Lower-bound | 1193.906 | 19.000 | 62.837 | | |

***TABLE 6. ENERGY EXPENDITURE***

Within-Subjects Factors

Measure: MEASURE_1

| factor1 | Dependent Variable |
|---|---|
| 1 | Control |
| 2 | Accumulation |
| 3 | Long |

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| kcal | 351.1476 | 158.08324 | 17 |
| kcal | 348.5127 | 134.52595 | 17 |
| kcal | 335.1320 | 149.57411 | 17 |

***TABLE 6. (CONTINUED) ENERGY EXPENDITURE***

Tests of Within-Subjects Effects

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power(a) |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 2507.407 | 2 | 1253.704 | .104 | .902 | .006 | .208 | .065 |
| | Greenhouse-Geisser | 2507.407 | 1.915 | 1309.688 | .104 | .894 | .006 | .199 | .064 |
| | Huynh-Feldt | 2507.407 | 2.000 | 1253.704 | .104 | .902 | .006 | .208 | .065 |
| | Lower-bound | 2507.407 | 1.000 | 2507.407 | .104 | .751 | .006 | .104 | .061 |
| Error (factor1) | Sphericity Assumed | 386376.679 | 32 | 12074.271 | | | | | |
| | Greenhouse-Geisser | 386376.679 | 30.632 | 12613.454 | | | | | |
| | Huynh-Feldt | 386376.679 | 32.000 | 12074.271 | | | | | |
| | Lower-bound | 386376.679 | 16.000 | 24148.542 | | | | | |

a Computed using alpha = .05

***TABLE 7. ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlation between systolic blood pressure reduction and changes in sympathetic modulation for the accumulation of short bouts of exercise treatment

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| accumulation-SBP | 5.3472 | 7.86441 | 18 |
| LF-accum | -.4367 | 7.70056 | 18 |
| HF-accum | .6083 | 6.22529 | 18 |
| ratio-accum | -.4017 | 1.41884 | 18 |

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlations

| | | accumulation-SBP | LF-accum | HF-accum | ratio-accum |
|---|---|---|---|---|---|
| accumulation-SBP | Pearson Correlation | 1 | .517(*) | -.503(*) | .381 |
| | Sig. (2-tailed) | | .028 | .033 | .119 |
| | N | 18 | 18 | 18 | 18 |
| LF-accum | Pearson Correlation | .517(*) | 1 | -.981(**) | .739(**) |
| | Sig. (2-tailed) | .028 | | .000 | .000 |
| | N | 18 | 18 | 18 | 18 |
| HF-accum | Pearson Correlation | -.503(*) | -.981(**) | 1 | -.734(**) |
| | Sig. (2-tailed) | .033 | .000 | | .001 |
| | N | 18 | 18 | 18 | 18 |
| ratio-accum | Pearson Correlation | .381 | .739(**) | -.734(**) | 1 |
| | Sig. (2-tailed) | .119 | .000 | .001 | |
| | N | 18 | 18 | 18 | 18 |

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Accumulation-SBP = systolic blood pressure reduction (mm Hg) following the accumulation of short bouts of exercise, LF-accum = changes in normalized low frequency power (%) following the accumulation of short bouts of exercise, HF-accum = changes in normalized high frequency power (%) following the accumulation of short bouts of exercise, ratio-accum = changes in ratio of low to high frequency power (%) following the accumulation of short bouts of exercise

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlation between diastolic blood pressure reduction and changes in sympathetic modulation for the accumulation of short bouts of exercise treatment

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| Accumulation-DBP | 3.4056 | 6.08170 | 18 |
| LF-DBP-10hr accum | -.3911 | 8.74618 | 18 |
| HF-DBP | .5383 | 6.99793 | 18 |
| ratio-DBP | -.4867 | 1.59268 | 18 |

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlations

| | | Accumulation-DBP | LF-DBP-10hr accum | HF-DBP | ratio-DBP |
|---|---|---|---|---|---|
| Accumulation-DBP | Pearson Correlation | 1 | .745(**) | -.738(**) | .756(**) |
| | Sig. (2-tailed) | | .000 | .000 | .000 |
| | N | 18 | 18 | 18 | 18 |
| LF-DBP-10hr accum | Pearson Correlation | .745(**) | 1 | -.983(**) | .754(**) |
| | Sig. (2-tailed) | .000 | | .000 | .000 |
| | N | 18 | 18 | 18 | 18 |
| HF-DBP | Pearson Correlation | -.738(**) | -.983(**) | 1 | -.763(**) |
| | Sig. (2-tailed) | .000 | .000 | | .000 |
| | N | 18 | 18 | 18 | 18 |
| ratio-DBP | Pearson Correlation | .756(**) | .754(**) | -.763(**) | 1 |
| | Sig. (2-tailed) | .000 | .000 | .000 | |
| | N | 18 | 18 | 18 | 18 |

** Correlation is significant at the 0.01 level (2-tailed).

Accumulation-DBP = diastolic blood pressure reduction (mm Hg) following the accumulation of short bouts of exercise, LF-DBP-10hr accum = changes in normalized low frequency power (%) following the accumulation of short bouts of exercise, HF-DBP = changes in normalized high frequency power (%) following the accumulation of short bouts of exercise, ratio-DBP = changes in ratio of low to high frequency power (%) following the accumulation of short bouts of exercise

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlation between systolic blood pressure reduction and changes in sympathetic modulation for a long bout of exercise treatment

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| Long-SBP | 5.9756 | 7.28566 | 18 |
| LF-long | -1.0617 | 10.35496 | 18 |
| HF-long | 1.3050 | 7.98753 | 18 |
| ratio-long | -.4083 | 1.98504 | 18 |

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlations

| | | Long-SBP | LF-long | HF-long | ratio-long |
|---|---|---|---|---|---|
| Long-SBP | Pearson Correlation | 1 | .374 | -.303 | .236 |
| | Sig. (2-tailed) | | .126 | .222 | .345 |
| | N | 18 | 18 | 18 | 18 |
| LF-long | Pearson Correlation | .374 | 1 | -.989(**) | .759(**) |
| | Sig. (2-tailed) | .126 | | .000 | .000 |
| | N | 18 | 18 | 18 | 18 |
| HF-long | Pearson Correlation | -.303 | -.989(**) | 1 | -.793(**) |
| | Sig. (2-tailed) | .222 | .000 | | .000 |
| | N | 18 | 18 | 18 | 18 |
| ratio-long | Pearson Correlation | .236 | .759(**) | -.793(**) | 1 |
| | Sig. (2-tailed) | .345 | .000 | .000 | |
| | N | 18 | 18 | 18 | 18 |

** Correlation is significant at the 0.01 level (2-tailed).

Long-SBP = systolic blood pressure reduction (mm Hg) following a long bout of exercise, LF-long = changes in normalized low frequency power (%) following a long bout of exercise, HF-long = changes in normalized high frequency power (%) following a long bout of exercise, ratio-long = changes in ratio of low to high frequency power (%) following a long bout of exercise

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlation between diastolic blood pressure reduction and changes in sympathetic modulation for a long bout of exercise treatment

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| Long-DBP | 3.3078 | 5.64307 | 18 |
| LF-long | -1.0617 | 10.35496 | 18 |
| HF-long | 1.3050 | 7.98753 | 18 |
| ratio-long | -.4083 | 1.98504 | 18 |

***TABLE 7. (CONTINUED) ASSOCIATION BETWEEN CHANGES IN SYMPATHETIC MODULATION AND BLOOD PRESSURE REDUCTION***

Correlations

| | | Long-DBP | LF-long | HF-long | ratio-long |
|---|---|---|---|---|---|
| Long-DBP | Pearson Correlation | 1 | .382 | -.371 | .543(*) |
| | Sig. (2-tailed) | | .118 | .130 | .020 |
| | N | 18 | 18 | 18 | 18 |
| LF-long | Pearson Correlation | .382 | 1 | -.989(**) | .759(**) |
| | Sig. (2-tailed) | .118 | | .000 | .000 |
| | N | 18 | 18 | 18 | 18 |
| HF-long | Pearson Correlation | -.371 | -.989(**) | 1 | -.793(**) |
| | Sig. (2-tailed) | .130 | .000 | | .000 |
| | N | 18 | 18 | 18 | 18 |
| ratio-long | Pearson Correlation | .543(*) | .759(**) | -.793(**) | 1 |
| | Sig. (2-tailed) | .020 | .000 | .000 | |
| | N | 18 | 18 | 18 | 18 |

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Long-DBP = diastolic blood pressure reduction (mm Hg) following a long bout of exercise, LF-long = changes in normalized low frequency power (%) following a long bout of exercise, HF-long = changes in normalized high frequency power (%) following a long bout of exercise, ratio-long = changes in ratio of low to high frequency power (%) following a long bout of exercise

***TABLE 8. BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

Systolic blood pressure

Within-Subjects Factors

Measure: MEASURE_1

| factor1 | Dependent Variable |
|---|---|
| 1 | baseline |
| 2 | first |
| 3 | second |
| 4 | third |

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| baseline | 126.5787 | 10.55943 | 20 |
| first | 124.8961 | 10.82745 | 20 |
| second | 123.8289 | 10.48500 | 20 |
| third | 122.8502 | 10.28020 | 20 |

***TABLE 8. (CONTINUED) BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

Systolic blood pressure

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power[a] |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assume | 179.762 | 3 | 59.921 | 2.979 | .039 | .136 | 8.936 | .675 |
| | Greenhouse-Geiss | 179.762 | 2.352 | 76.426 | 2.979 | .053 | .136 | 7.006 | .595 |
| | Huynh-Feldt | 179.762 | 2.706 | 66.441 | 2.979 | .045 | .136 | 8.059 | .640 |
| | Lower-bound | 179.762 | 1.000 | 179.762 | 2.979 | .101 | .136 | 2.979 | .374 |
| Error(factor1 | Sphericity Assume | 1146.618 | 57 | 20.116 | | | | | |
| | Greenhouse-Geiss | 1146.618 | 44.690 | 25.657 | | | | | |
| | Huynh-Feldt | 1146.618 | 51.406 | 22.305 | | | | | |
| | Lower-bound | 1146.618 | 19.000 | 60.348 | | | | | |

a. Computed using alpha = .05

***TABLE 8. (CONTINUED) BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

Diastolic blood pressure

Within-Subjects Factors

Measure: MEASURE_1

| factor1 | Dependent Variable |
|---|---|
| 1 | baselineDBP |
| 2 | firstDBP |
| 3 | secondDBP |
| 4 | thirdDBP |

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| DBP-15 min | 80.9545 | 8.42645 | 20 |
| firstDBP | 81.1885 | 10.76894 | 20 |
| secondDBP | 82.2915 | 8.38196 | 20 |
| thirdDBP | 81.6255 | 7.78639 | 20 |

***TABLE 8. (CONTINUED) BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE***

***TREATMENT***

Diastolic blood pressure

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power[a] |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 20.718 | 3 | 6.906 | .580 | .630 | .030 | 1.741 | .163 |
| | Greenhouse-Geisse | 20.718 | 2.123 | 9.759 | .580 | .574 | .030 | 1.232 | .142 |
| | Huynh-Feldt | 20.718 | 2.397 | 8.643 | .580 | .594 | .030 | 1.391 | .149 |
| | Lower-bound | 20.718 | 1.000 | 20.718 | .580 | .456 | .030 | .580 | .112 |
| Error(factor1 | Sphericity Assumed | 678.502 | 57 | 11.904 | | | | | |
| | Greenhouse-Geisse | 678.502 | 40.336 | 16.821 | | | | | |
| | Huynh-Feldt | 678.502 | 45.548 | 14.896 | | | | | |
| | Lower-bound | 678.502 | 19.000 | 35.711 | | | | | |

a. Computed using alpha = .05

***TABLE 9. HEART RATE VARIABILITY FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE TREATMENT***

Normalized low frequency power (%)

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| LF0 | 79.9633 | 5.91251 | 20 |
| LF1 | 80.0622 | 10.21451 | 20 |
| LF2 | 80.1081 | 11.51311 | 20 |
| LF3 | 78.5807 | 15.26631 | 20 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power[a] |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 32.363 | 3 | 10.788 | .160 | .923 | .008 | .479 | .078 |
| | Greenhouse-Geisser | 32.363 | 2.319 | 13.958 | .160 | .881 | .008 | .370 | .075 |
| | Huynh-Feldt | 32.363 | 2.660 | 12.167 | .160 | .905 | .008 | .425 | .076 |
| | Lower-bound | 32.363 | 1.000 | 32.363 | .160 | .694 | .008 | .160 | .067 |
| Error(factor1) | Sphericity Assumed | 3851.746 | 57 | 67.574 | | | | | |
| | Greenhouse-Geisser | 3851.746 | 44.053 | 87.435 | | | | | |
| | Huynh-Feldt | 3851.746 | 50.538 | 76.214 | | | | | |
| | Lower-bound | 3851.746 | 19.000 | 202.723 | | | | | |

a. Computed using alpha = .05

LF = normalized low frequency power (%), 0 = baseline, 1= rest period following the 1st short session of exercise, 2 = rest period following the 2nd short session of exercise, 3 = rest period following the 3rd session of exercise

***TABLE 9. (CONTINUED) BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE***

***TREATMENT***

Normalized high frequency power (%)

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| HF0 | 17.9365 | 5.05739 | 20 |
| HF1 | 17.7557 | 9.22561 | 20 |
| HF2 | 17.7989 | 10.29109 | 20 |
| HF3 | 19.1397 | 13.68188 | 20 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power[a] |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 26.071 | 3 | 8.690 | .153 | .927 | .008 | .459 | .077 |
| | Greenhouse-Geisser | 26.071 | 2.384 | 10.936 | .153 | .891 | .008 | .365 | .074 |
| | Huynh-Feldt | 26.071 | 2.749 | 9.484 | .153 | .914 | .008 | .421 | .075 |
| | Lower-bound | 26.071 | 1.000 | 26.071 | .153 | .700 | .008 | .153 | .066 |
| Error(factor1) | Sphericity Assumed | 3234.420 | 57 | 56.744 | | | | | |
| | Greenhouse-Geisser | 3234.420 | 45.294 | 71.409 | | | | | |
| | Huynh-Feldt | 3234.420 | 52.231 | 61.925 | | | | | |
| | Lower-bound | 3234.420 | 19.000 | 170.233 | | | | | |

a. Computed using alpha = .05

HF = normalized high frequency power (%), 0 = baseline, 1= rest period following the 1st short session of exercise, 2 = rest period following the 2nd short session of exercise, 3 = rest period following the 3rd session of exercise

***TABLE 9. (CONTINUED) BLOOD PRESSURE FOLLOWING SUCCESSIVE SHORT SESSIONS OF EXERCISE***

***TREATMENT***

Ratio of low to high frequency power

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| ratio0 | 4.9182 | 1.86221 | 20 |
| ratio1 | 5.9845 | 3.62330 | 20 |
| ratio2 | 6.2855 | 4.08153 | 20 |
| ratio3 | 6.7087 | 4.56857 | 20 |



**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. | Partial Eta Squared | Noncent. Parameter | Observed Power[a] |
|---|---|---|---|---|---|---|---|---|---|
| factor1 | Sphericity Assumed | 35.034 | 3 | 11.678 | 1.477 | .230 | .072 | 4.431 | .370 |
| | Greenhouse-Geisser | 35.034 | 2.544 | 13.772 | 1.477 | .236 | .072 | 3.757 | .337 |
| | Huynh-Feldt | 35.034 | 2.970 | 11.795 | 1.477 | .231 | .072 | 4.387 | .368 |
| | Lower-bound | 35.034 | 1.000 | 35.034 | 1.477 | .239 | .072 | 1.477 | .211 |
| Error(factor1) | Sphericity Assumed | 450.670 | 57 | 7.906 | | | | | |
| | Greenhouse-Geisser | 450.670 | 48.334 | 9.324 | | | | | |
| | Huynh-Feldt | 450.670 | 56.434 | 7.986 | | | | | |
| | Lower-bound | 450.670 | 19.000 | 23.719 | | | | | |

a. Computed using alpha = .05

ratio = ratio of low to high frequency power, 0 = baseline, 1= rest period following the 1st short session of exercise, 2 = rest period following the 2nd short session of exercise, 3 = rest period following the 3rd session of exercise

***TABLE 10. CORRELATION BETWEEN SYSTOLIC BLOOD PRESSURE REDUCTION DURING THE REST PERIOD FOLLOWING SHORT SESSIONS AND SYSTOLIC BLOOD PRESSURE REDUCTION FOLLOWING THE ACCUMULATION OF SHORT BOUTS OF EXERCISE***

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---|---|---|---|
| accumulation reduction | 5.3555 | 7.58854 | 20 |
| ave reduction | 3.2810 | 5.60654 | 20 |

Correlations

| | | accumulation reduction | ave reduction |
|---|---|---|---|
| accumulation reduction | Pearson Correlation | 1 | .135 |
| | Sig. (2-tailed) | | .581 |
| | N | 20 | 19 |
| ave reduction | Pearson Correlation | .135 | 1 |
| | Sig. (2-tailed) | .581 | |
| | N | 19 | 20 |

Accumulation reduction = average systolic blood pressure reduction following the accumulation of short bouts of exercise (mm Hg), ave reduction = average systolic blood pressure reduction during rest periods following three short sessions

## *APPENDIX E - REVIEW AND APPROVAL OF RESEARCH PROJECT UTILIZING HUMAN SUBJECTS*

## *NOTICE OF APPROVAL – FULL COMMITTEE REVIEW*

INDIANA UNIVERSITY

**NOTICE OF APPROVAL**
**FULL COMMITTEE REVIEW**

**TO:** Saejong Park
HPER

**DATE:** November 1, 2003

RESEARCH AND THE UNIVERSITY GRADUATE SCHOOL

**FROM:** Cybil Cole, Director Human Subjects Risk Compliance

**RE:** Protocol entitled: Accumulation of Three Short Bouts of Brisk Walking on Blood Pressure Reduction in Hypertension
Protocol #: 03- 8515

The Human Subjects Committee (HSC) has reviewed and approved the research protocol referenced above. As the principal investigator of this study you assume the following reporting responsibilities:

**CONTINUING REVIEW:** A status report must be filed with the committee. You are required to apply for renewal of approval at least once a year for as long as the study is active. All projects will automatically receive a renewal notice from the HSC. **This study is approved from October 31, 2003 to October 30, 2004.**

**AMENDMENTS:** Investigators are required to report on these forms **ANY** changes to the research study (such as design, procedures, consent forms, or subject population, including size). An amendment form is attached for your future use. ***The new procedure may not be initiated until HSC approval has been given.***

**AUDIT OR INSPECTION REPORTS:** Investigators are required to provide to the HSC a copy of any audit or inspection reports or findings issued to them by regulatory agencies, cooperative research groups, contract research organizations, the sponsor, or the funding agency.

**COMPLETION:** You are required to notify the HSC office when your study is completed (data collection finished). Please contact the HSC office for the appropriate form to use.

**ADVERSE REACTIONS:** If any unexpected adverse reactions occur as a result of this study, you must notify the HSC Office immediately. A written report must be filed within 3 working days.

**CONSENT FORMS:** All subjects should be given a copy of **the stamped approved** consent form. You must retain signed consent documents for at least three years past completion of the research activity.

We suggest you keep this letter with your copy of the approved protocol. Please refer to the exact project title and protocol number in any future correspondence with our office. All correspondence must be typed.

Enclosures: Documentation of Review and Approval
Amendment Form
Approved Consent Form- **stamped copy must be used**

Federal Wide Assurance #FWA00003544-IRB00000222
For additional FWA information, see the Web site at
http://www.iupui.edu/~resgrad/spon/fwa.htm

BLOOMINGTON CAMPUS COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS

Indiana University
Bryan Hall, Room 110
107 South Indiana Avenue
Bloomington, Indiana
47405-7000

812-855-3067
Fax: 812-855-6396
E-mail:
iub_hsc@indiana.edu
WWW Address:
http://www.indiana.edu/~resrisk.html

## *DOCUMENTATION OF REVIEW AND APPROVAL*

**INDIANA UNIVERSITY**
**BLOOMINGTON CAMPUS COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS**

**DOCUMENTATION OF REVIEW AND APPROVAL**
of
Research Project Utilizing Human Subjects

RECEIVED
SEP 29 2003
HUMAN SUBJECTS COMMITTEE

Study # 03-8515

TITLE OF PROJECT Accumulation of three short bouts of brisk walking on blood pressure reduction in hypertension

PROJECT DURATION - START DATE October 31 2003 END DATE October 31 2004

PRIN. INVESTIGATOR Saejong Park SCHOOL/DEPARTMENT HPER/Kinesiology

ADDRESS 808 Woodbridge Dr. Bloomington, IN 47408 E-MAIL saejpark@indiana.edu PHONE 812-333-8249

RANK: Faculty ___ Res. Scientist ___ Post-Doc ___ Staff ___ Student: undergrad ___ masters ___ PhD/EdD X

**If PI's rank is OTHER than faculty, name of faculty overseeing the research** (SPONSOR) Janet P. Wallace, Ph.D

SPONSOR'S E-MAIL & CAMPUS ADDRESS wallacej@indiana.edu /HPER Rm.112-G PHONE 812-855-6384

FUNDING AGENCY_____ APPL. DEADLINE_____

AGENCY PROJECT # _____ New _____ Continuation

*As the principal investigator, my signature testifies that I pledge to conform to the following:*

As one engaged in investigation utilizing human subjects, I acknowledge the rights and welfare of the human subject involved.

I acknowledge my responsibility as an investigator to secure the informed consent of the subject by explaining the procedures, in so far as possible, and by describing the risks as weighed against the potential benefits of the investigation.

I assure the Committee that all procedures performed under the project will be conducted in accordance with those Federal regulations and University policies which govern research involving human subjects. **Any deviation from the project (e.g., change in principal investigator, research methodology, subject recruitment procedures, etc.) will be submitted to the Committee in the form of an amendment for its approval prior to implementation.**

PRINCIPAL INVESTIGATOR:

Saejong Park _____ _____ _____
(typed/printed name) (signature) (date)

***As the faculty sponsor, my signature testifies that I have reviewed this application and that I will oversee the research in its entirety, through the termination report.***

FACULTY SPONSOR:

Janet P. Wallace _____ _____ _____
(typed/printed name) (signature) (date)

**********

**CAMPUS LEVEL REVIEW**

This protocol for the use of human subjects has been reviewed and approved by the Indiana University/Bloomington Campus Committee for the Protection of Human Subjects.

_____ Exempt Review ¶#_____, _____ Exempt ¶# _____ with signed/documentation of consent,

_____ Expedited Review ¶#_____, _____ Full Review, _____ Not Approved, _____ Withdrawn

_____ _____
Chairperson/Agent IUB Committee Date

logged in ts _____ approval logged _____ copy to PI _____ notice to SOE _____ rank code _____

test: PI _____ sponsor _____ co-PI _____

## *EXPEDITED/FULL REVIEW CHECKLIST*

**DIRECTIONS:** This form is to be completed and submitted to the Committee when the investigator plans a research project which, in the investigator's judgment, requires expedited or full Committee review. Items 1-7 are the categories which **may** qualify for expedited review. ***If "yes" is the response to any of items 10-13, the study will most likely require full Committee review.***

STUDIES INVOLVING *minors, pregnant women, fetuses, prisoners, persons with mental disabilities and economically or educationally disadvantaged persons* **MAY**, IN THE DISCRETION OF THE CHAIR, REQUIRE FULL COMMITTEE REVIEW.

**APPLICABILITY:**

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve ONLY procedures listed in one or more of the following categories, may be reviewed by HSC through the expedited review procedures authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedures when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review.

**CIRCLE THE APPROPRIATE CATEGORY NUMBERS THAT APPLY TO YOUR RESEARCH PROJECT AND UNDERLINE, OR HIGHLIGHT, THE SPECIFIC SECTION WITHIN EACH CATEGORY.**

1. Clinical studies of drugs and medical devices only when condition (a) **OR** (b) is met.

   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture **as follows**:

(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week; **OR**

(b) from other adults and children* considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

**A 20-45ml sample of venous blood for hypertensive adults will be drawn by a certified technician via sterile techniques for analysis of cholesterol, triglycerides, glucose, and various electrolytes and enzymes. This blood draw will take place at the Indiana University Health Center.**

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**EXPEDITED/FULL REVIEW CHECKLIST continued**

3. Prospective collection of biological specimens for research purposes by noninvasive means.

**Examples of biological specimens:** (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or it routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated (not by a tube inserted into the mouth) saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

**Examples of procedures:** (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler

blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(3). This listing refers only to research that is not exempt.)

8. Use of minors under age 18, or economically or educationally disadvantaged persons.

9. Use of deception. (See item 14 on page 11.)

10. ***Use of prisoners, pregnant women, fetuses, the seriously ill, or persons with mental disabilities, or incompetent individuals.***

11. ***Collection of information or recording of behavior which, if known outside of the research, could reasonably place the subject at risk of civil or criminal liability or damage the subject's financial standing, employability, insurability, reputation, or be stigmatizing.***

12. ***Collection of information regarding sensitive aspects of the subject's behavior such as: drug and alcohol use, illegal conduct, or sexual behavior.***

13. ***This project includes procedures that present more than minimal risk to the subject.***

14. This project includes procedures not listed above.

* Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).
2/00;www;msw

## *SUMMARY SAFEGUARD STATEMENT*

Project Title (if you wish to use a different title in the consent statement than is listed on page 3, explain here):

Accumulation of three short bouts of brisk walking on blood pressure reduction in hypertension

IF ADDITIONAL SPACE FOR RESPONSES IS DESIRED, THIS DOCUMENT MAY BE
RETYPED ONTO PLAIN PAPER MAINTAINING THE IDENTICAL ORDER AND EXACT
QUESTION WORDING WHILE ADDING EXTRA SPACE WHERE NEEDED.

**Do not type on the reverse side of any form.**
**Use type size no smaller than ARIAL 11 or TIMES NEW ROMAN 12 point.**

A. Briefly describe, in lay terms, the general nature and purpose of the proposed research, and where the study will take place. If student research, indicate whether for a course, thesis, dissertation, or independent research. If the study is only for a course, please review the Student Research Policy to ascertain if this project requires HSC review.

*More than 50 millions of Americans have high blood pressure. Exercise is one of the most promising lifestyle modifications for treatment of high blood pressure. A single exercise treatment significantly decreases 5-8 mmHg of systolic blood pressure for 11 to 13 hours and 6-8mmHg of diastolic blood pressure for 4 to 9 hours. However, trends toward participation of exercise appear to be stabilizing or reversing. One of the primary barriers to exercise is the lack of time and amount of time consumed at exercise. For many individuals short bouts of exercise may fit better into a busy schedule than a single long bout of exercise. Accumulating short bouts of exercise has been found to improve fitness. Thus, accumulating exercise in daily life has been widely recommended by Surgeon General, American Heart Association, and American College of Sports and Medicine to improve fitness or decrease the risk of heart disease. Accumulating short bouts of exercise is also recommended as a treatment for high blood pressure. However, there is no study to support the effects of accumulating exercise as a treatment for high blood pressure.*

*The purpose of the study is (1) to describe the magnitude and duration of blood pressure reduction following each successive short bout (15 minutes) of brisk walking, (2) to compare the magnitude and duration of the blood pressure reduction following the accumulation of short bouts of brisk walking to the magnitude and duration of the blood pressure reduction following a single long bout of brisk walking, (3) to investigate the possible mechanism (sympathetic modulation analyzed by ambulatory electrocardiogram, EKG monitor) of the blood pressure reduction following each successive short bouts of brisk walking, and (4) to compare the possible mechanism of the blood pressure reduction following the accumulation of short bouts of brisk walking to the possible mechanism of the blood pressure reductions following a single long bout of brisk walking in hypertensive adults. It is hypothesized that the blood pressure reduction following the accumulation of three short bouts of brisk walking will be more effective than a single long bout of brisk walking in hypertension. It is also hypothesized that the possible mechanism of blood pressure reduction following exercise will be changes in the nervous control of blood pressure regulation (or*

*changes in the sympathetic modulation using heart rate variability measured by ambulatory EKG monitor).*

*This study will be conducted in the Clinical Exercise Physiology of the Human Performance Laboratories in the Department of Kinesiology, School of HPER.*

*This study is student research for doctoral dissertation.*

B. Describe the process by which subjects will be recruited (see item F on page 2), how many (or estimate) subjects will be involved in the research, and how much time will be required of them. List specific eligibility requirements for subjects (or describe screening procedures), including those criteria that would exclude otherwise acceptable subjects. If your study uses only male or female subjects, explain why. For NIH-funded research only, address the inclusion of women, minorities and children in the research. Disclose any relationship between researcher and subjects - such as, teacher/student; superintendent/principal/teacher; employer/employee (see Students as Subjects section in the Policy Manual).

*The recruitment process will start with letters to local physicians (attached). These letters will inform the primary physicians of the study, define their roles, and ask for assistance in recruiting subjects. Public service announcements (attached) on local radio stations and press releases in the local newspaper will serve as additional means for subject recruitment. Information will be given at local health fairs and some subjects will be recruited from the Indiana University Adult Fitness Program.*

*Approximately 18 hypertensive adults will be involved in this study.*

*The total required time for each subject will be 7-8 hours over 21 to 30 day period.*

*(1) Blood pressure screening (15 minutes)*
*(2) First day of laboratory testing (1-1.5 hours)*
*a. Resting blood pressure measurements*
*b. Resting 12-lead electrocardiogram (EKG)*
*c. Pulmonary function tests (for smokers only)*
*d. Fasting venous blood draw at IU Health Center*
*(3) Second day of laboratory testing (2 hours)*
*a. Resting blood pressure measurements*
*b. Second resting 12-lead EKG*
*c. Maximal graded exercise test*
*(4) 24-hour ambulatory blood pressure and EKG monitoring trials (3 hours)*
*a. On a day following three short bouts (15 minutes) of exercise*
*b. On a day following a long bout (45 minutes) of exercise*
*c. On a day of the control without exercise (20 minutes)*

*Subjects will be hypertensive adults (18 years or older). Hypertensive adults will be defined by one of the following: 1) having had a previous diagnosis of hypertension by a primary physician; 2) having a mean systolic blood pressure ≥140 mmHg and/or a mean diastolic blood pressure ≥90 mmHg taken from at least two readings on two separate days, three days apart, or 3) exhibiting a mean daytime ambulatory blood pressure of ≥135/85 mmHg. Subject exclusion will include 1) significant cardiovascular disease, 2) significant dysrhythmia, 3) brachial artery bruits, 4) cardiac or renal transplant patients, 5) treatment with antihypertnesive medications, and 6) sleep apnea. A physician clearance by the subject's primary physician will be required for every subject prior to participation*

*in the study (form attached). Hypertensive subjects who are taking antihypertensive medications will be taken off medications with approval of their primary physician. Blood pressure screening for subjects going off anti-hypertensive medications will be continued on a daily basis for the first week of withdrawal to every other day thereafter. Subjects will be referred back to their primary physician to resume medications and withdraw from the study if the screening blood pressures exceed the criterion blood pressure measurement (>3 days in a row) determined by the primary physician.*

*The relationship between subjects and investigators is researcher-subject.*

C. Check appropriate box for type of vulnerable subject population involved when investigation specifically studies: **N/A**
[_] minors (under age 18), [_] fetuses, [_] pregnant women, [_] persons with mental disabilities,
[_] prisoners, [_] persons with physical disabilities, [_] economically or educationally disadvantaged,
[_] other vulnerable population.

If any of the above are used, state the necessity for doing so. Please indicate the approximate age range of the minors to be involved.

D. List all procedures to be used on human subjects or describe what subjects will do. If done during regular class time, explain what non-participants will do. If you are taping, explain that here (see item 13 on page 11). *Asterisk* those you consider experimental. For those asterisked procedures, describe the usual method(s), if any, that were considered and why they were not used. (See item F on page 2 for more information.)

*Subjects will be asked to complete a blood pressure screening following by two sets of laboratory testing. Because this study is a within-subjects design, each subject will experience all three of 24-hour ambulatory blood pressure and EKG monitoring trials; one on a control day without exercise, and two on days with exercise (three short bouts (15 minutes) of brisk walking and a long bout (45 minutes) of brisk walking).*

*Procedures include*
***1) Blood pressure screening***
*Subject will be seated at least 5 minutes in a chair with his/her back supported and arms bared and supported heart level prior to a blood pressure screening. A blood pressure screening will consist of three blood pressure measurements on two separate days, at least three days apart (a total of six measurements). On the first day of screening, blood pressure will be taken on both arms. The arm with the higher blood pressure will be used for the screening on the second day and for the calculation of the average of the six screening pressures.*
*Blood pressure screening for subjects going off anti-hypertensive medications will be continued on a daily basis for the first week of withdrawal to every other day thereafter. Subjects will be referred back to their primary physician to resume medications and withdraw from the study if the screening blood pressures exceed the criterion blood pressure measurement (>3 days in a row) determined by the primary physician.*

***2) First day of laboratory testing:***

***a. Resting 12-lead EKG***

Subject will lie on a cot and have electrodes attached to his/her arms, legs, and chest to observe the electrical activity of the heart. Subject will also be asked to breathe deeply for 20 seconds to observe how deep breathing affects his/her EKG.

***b. Pulmonary function tests (for smokers only)***

*Subject will breathe in and out as hard and fast as he/she can with room air through hoses attached to the computer to determine the capacity of his/her lung. This will be done for smokers to assure that lung function will not limit the ability to do exercise.*

***c. Fasting venous blood draw at IU Health Center***

*Subject will be asked to be fasting at least for 12 hours prior to blood draw. All blood sampling will take place at IU Health Center. All samples will be collected by laboratory technologists certified in phlebotomy. The amount of whole blood drawn is minute, 20-45 ml. The efficacy of cardiovascular or hemodynamic mechanisms and arterial pressure are not compromised with these volumes of blood draw.*

***3) Second day of laboratory testing:***

***a. Second resting 12-lead EKG***

Before a maximal graded exercise test, subject will lie on a cot and have electrodes attached to his/her shoulder, hip, and chest to observe the electrical activity of the heart in a lying position. Then, subject will be asked to stand up to record EKG in an upright position. This second EKG will be compared to the previous EKG to see any recent significant changes occurred.

***b. Maximal graded exercise test***

*This test is designed to measure subject's fitness and cardiovascular response to exercise. Subject will walk on a motor-driven treadmill with the grade or slope increasing progressively until fatigue, breathlessness, chest discomfort, and/or any other symptoms which indicate to a medical doctor, technicians or subject him/herself that he/she should stop exercise. Heart rate, EKG and blood pressure will be monitored through the test. Subject's expired gases will be also collected through mouthpiece either throughout the test or at the end of the test. A medical doctor will be present and supervising the entire test.*

***4) Measurements of 24-hour ambulatory blood pressure and EKG monitoring trials:***

***a. Following three short bouts of Exercise treatment***

***b. Following a long bout of exercise treatment***

***c. Following a control treatment (without exercise)***

***Exercise Treatments***

*The long bout (45 minutes) of exercise treatment will be administered between 6am and 8am. The first session of an accumulating three short bouts (15 minutes) of exercise treatment will be administered between 6am and 8am, the second between 11am and 1pm and the third between 4pm and 6pm. Each exercise treatment will be 45 minutes. Each exercise treatment will consist of walking on a motor driven treadmill at 50% of maximal oxygen uptake ($VO_2$max), which will be obtained by the maximal exercise test. That is, the speed and grade form the stage of the test that is elicited 50 % of $VO_2$max will be used for the exercise stimulus. $VO_2$ will be measured during the $4^{th}$ through the $6^{th}$ minutes to confirm the exercise stimulus. The work rate will be adjusted if it is not within $\pm$10% of the target oxygen uptake. $VO_2$ will then be measured during the $10^{th}$*

*through the 12th minutes of the work to confirm the new exercise intensity. Heart rate (via ECG) will be measured every minute during the exercise session; blood pressure (via auscultation) will be measured every 2 to 5 minutes.*

***24-hour Ambulatory Blood Pressure and EKG Monitoring***

*Ambulatory 24-hour blood pressure and EKG (Holter) will be taken, starting in the morning following both the exercise and control treatments. The order of presentation of the three short bouts and a long bout of exercise treatments as well as a control treatment will be randomized. The two exercise treatments will be greater than 7 days apart to avoid training effect.*

*The Accutracker II will be used for ambulatory 24-hour blood pressure measurements. The sampling interval will be randomized to take a reading on the average of every 15 $\pm$5 minutes for daytime hours (6 am to 10 pm) and on the average of every 30 $\pm$5 minutes for nighttime hours (10 pm to 6 am). One repeat measurement will be taken if the first measurement is unsuccessful during the daytime hours and two repeat measurements will be taken during the nighttime hours. The cuff inflation cuff for each measurement will be 30 mmHg greater than the previous reading. The cuff deflation will be set at 3 mmHg/second. The blood pressure cuff will be worn on the non-dominant arm. Four EKG electrodes will be placed in the chest. Electrode wires and blood pressure tubing will be taped securely to the chest. The subject will be given the option to secure a small box, recording unit with a belt or the shoulder strap provided. A roll of micropore tape and new electrodes will be given to each subject to re-tape areas or to replace electrodes if needed.*

*The DigiCorder will be used for 24-hour electrocardiogram or EKG recording. Subject will get seven electrodes attached to his/her chest and will carry a small box on a belt or shoulder strap. Electrode wires will be taped securely to the chest. A roll of micropore tape and new electrodes will be given to each subject to re-tape areas or to replace electrodes (picture will be given) if needed. When the data from DigiCorder is downloaded, the changes in the nervous control of blood pressure regulation using heart rate variability software (Del Mar Medical systems, LLC) will be obtained. This measurement will be performed to investigate the mechanism of blood pressure reductions resulted from different exercise treatments.*

*Subjects will be asked to document 1) time of sleep, 2) time at work, 3) time of meals, 4) time at leisure activities, and 5) any physical activities or exercise. Subjects will be instructed 1) not to get the monitor wet, 2) not to exercise, 3) not to take a shower, 4) not to use electric blanket, 5) not to operate a lawn mower, a vacuum cleaner or any equipment which would cause vibration, and 6) to relax and straighten out the arm during the blood pressure recording for the entire 24-hour period.*

*All of the laboratory testing protocols listed below have been previously approved for use in the Adult Fitness Program (97-21) and Blood Pressure Clinic as well as other studies involving hypertensive adults (97-1962, and Bogle, P.G. (2001) Hemodynamic determinants of post exercise hypotension: An ambulatory study). Saejong Park, P.I. has been performing the research (01-4483, Effects of morning and evening exercise treatments on the diurnal variation of blood pressure effects of exercise on hypertension) with similar procedures.*

E. State the potential risks - for example, physical, psychological, financial, social, legal or other - connected with the proposed procedures.

Briefly describe how risks to subjects are reasonable in relation to anticipated benefits. Describe procedures for protecting against, or minimizing, potential risks. Assess their likely effectiveness. If you are using an electrical device that is attached directly to subjects explain how the subjects will be protected from shock.

***1) Blood pressure screening***

*There are no major risks associated with a blood pressure screening. The risk associated* ***with temporary discontinuation of antihypertensive medication*** *is the return of blood pressure to pre-medication pressures.* ***The temporary discontinuation of antihypertensive medication*** *must be approved by the subject's primary physician (form included). During the discontinuation of medications the blood pressure will be monitored and recorded daily for the first week, and every other day thereafter by lab technicians. The primary physician will indicate the threshold blood pressure for resuming medication. If the subject reaches this threshold, the subject will be referred back to their primary care physician, encouraged to resume to taking antihypertensive medication and will be discontinued from the study.*

***2) First day of laboratory testing:***

***a. Resting 12-lead EKG***

***b. Pulmonary function tests (for smokers only)***

***c. Fasting venous blood draw at IU Health Center***

*There are no major risks associated with resting 12-lead EKG and pulmonary function tests. Light headiness is experienced by some people undergoing pulmonary tests. Subjects will be seated during pulmonary function tests to prevent episodes. To minimize the risk, trained staff/student personnel will give instructions and demonstrations in testing. Testing will be under the supervision of Janet P. Wallace, Ph.D. Each room of the Clinical Exercise Physiology Laboratory has two emergency buttons. The yellow light is for assistance and the red light is for emergencies. The physician's office, reception area, and the office of the Human performance Director have a panel that indicates which room and light is activated. Notification of emergency, action of personnel, and protocol can be communicated over the lab public address system.*

*The risks associated with venous draw are minimal: bruising, infection or soreness at the puncture site, and falls due to fainting. These risks will be minimized by having the blood drawn by a trained technician at the IU health center while subjects are seated. The amount of whole blood drawn is minute, 20-45 ml. The efficacy of cardiovascular or hemodynamic mechanisms and arterial pressure are not compromised with these volumes of draw or finger prick. Infectious waste are collected separately and stored in hazardous bags until disposal. Methods of disposal by incineration are performed by IU Health Center. There is a greater risk of contracting HIV virus for the technician than for the subject.*

***3) Second day of laboratory testing:***

***a. Second resting 12-lead EKG***

***b. Maximal graded exercise test***

*There are no major risks associated with resting 12-lead EKG. The discomforts associated with exercise treatment can include episodes of transient light headaches, occasional irregular heart beats, chest discomfort, abnormal blood pressure responses, musculoskeletal injury and sore muscles. Risks inherent in maximal graded exercise test range from traumatic events from falling on the treadmill to sudden death. The risk of cardiac event is 1 to 3 in 10,000 tests and the risk of death is 1 in 10, 000 tests for a high risk population.*

*Procedures for protecting against or minimizing, potential risks are described:*

*Trained staff/student personnel will give instructions and demonstrations in the testing. Standard procedures will be used for preparation, test administration, and test termination to minimize risk for maximal graded exercise test. Established criteria for the maximal graded test include: a physician approved clearance for participation, risk factor identification, resting 12 lead electrocardiogram (EKG), and instruction and practice to accustom the subject to the treadmill. Risk will be minimized during exercise testing with continuous monitoring of the EKG, heart rate, blood pressure and monitoring the signs and symptoms as well as maintaining constant communication with the subject (both visually and verbally). Prior physician approval serves as a preliminary screening for medical conditions and medical histories contraindicated for exercise testing. Risk factor identifications including family history, blood lipids, blood pressure, blood glucose, body composition, physical activity habits, age and sex determine the pre-test likelihood for coronary heart disease. This identification dictates physician supervision of testing, modification of the test protocol, and the frequency of monitoring variables during testing. The resting EKG screens prior silent infarcts and EKG changes from previous testing. Both are absolute and/or relative EKG contraindications for exercise testing. Treadmill instruction and practice will help the subject comfort walking or jogging. Continuous monitoring of variables during testing help detect early test termination points. This detection will help prevent potential cardiac events. Constant visual and verbal communication with the subject assures early detection and evaluation of symptoms which may develop during the testing such as chest discomfort, lightheadedness, and musculoskeletal problems.*

*Physician supervision is warranted for all hypertensive subjects during exercise testing. In other words, a physician will be present and supervising maximal graded exercise test for all the subjects. Criterion for physician supervision will be in accordance with ACSM Guidelines for Exercise Testing and Prescription. Individual risk status will be determined for each subject prior to the exercise test. This risk status will be based on subject responses on the Medical History/Health Habits Questionnaire, results of the physician examination, resting blood pressure, body composition analysis and fasting blood chemistry measurements. Classifications of risk status for adults include low, moderate and high risk. Subjects who present with any absolute contraindications to exercise will not be allowed to participate in this study. Subjects who present with relative contraindications can be tested provided the Medical Director or primary physician approves. Test termination for exercise testing will adhere to the ACSM Guidelines.*

*The exercise testing will also be under the supervision of the Medical Director, Larry Rink, M.D. All technicians have practiced the emergency protocol and participated in CPR classes three times a year. All technicians are certified (American Heart Association) in the use of an automatic external defibrillator (AED). In addition, a practice run will be coordinated with the ambulance service of Bloomington Hospital once a year.*

*Each room of the Clinical Exercise Physiology Laboratory has two emergency buttons. The yellow light is for assistance and the red light is for emergencies. The physician's office, reception area, and the office of the Human performance Director have a panel that indicates which room and light is activated. Notification of emergency, action of personnel, and protocol can be communicated over the lab public address system.*

***4) Measurements of 24-hour ambulatory blood pressure and Holter monitoring trials:***

***a. Following three short bouts of physical activity treatment***
***b. Following a long bout of physical activity treatments***
***c. The corresponding morning of the non-exercise control treatment.***

*There are no major risks for 24-hour ambulatory blood pressure monitoring. Discomforts include minor skin irritation from adhesive, possible sleep disturbances, minor discomfort of the arm during cuff inflation, possible disturbance of daily tasks, and rare events that include petechiae (tiny little broken capillary blood vessels), thrombophlebitis (formation of a blood clot inside an inflamed vein), edema, abrasions, and eccymoses (larger bruises). The risks will be minimized by inflating blood pressure cuff just little above (30 mmHg) the previous subject's blood pressure. Phone numbers of the investigators will be provided to the subjects if they have any problems with the device during the course of the monitoring.*

*There are no major risks for 24-hour ambulatory EKG monitoring. Discomforts include minor skin irritation from adhesive, possible sleep disturbances, and/or possible disturbance of daily tasks. Phone numbers of the investigators will be provided to the subjects if they have any problems with the device during the course of the monitoring.*

*The discomforts associated with exercise treatment (50% of amount of exercise from graded maximal exercise test) can include episodes of transient light headaches, occasional irregular heart beats, chest discomfort, abnormal blood pressure responses, musculoskeletal injury and sore muscles. The risk of heart attack, although small (1 to 3 in 10,000), does exist. Reasonable effort will be made to minimize risk through the use of proper warm-up, exercise, and cool-down techniques. Blood pressure and EKG will be monitored during exercise treatments by technicians. All technicians have practiced the emergency protocol and participated in CPR classes three times a year. All technicians are certified (American Heart Association) in the use of an automatic external defibrillator (AED). In addition, a practice run will be coordinated with the ambulance service of Bloomington Hospital once a year. Clinical Exercise Physiology Laboratory has two emergency buttons. The yellow light is for assistance and the red light is for emergencies. The physician's office, reception area, and the office of the Human performance Director have a panel that indicates which room and light is activated. Notification of emergency, action of personnel, and protocol can be communicated over the lab public address system.*

F. Describe methods for preserving confidentiality. How will data be recorded and stored, with or without identifiers? If identifiers are used describe the type: names, job titles, number code, etc. How long are identifiers kept? If coding system is used, is there a link back to the subject's ID? If yes, where is the code list stored in relation to data and when is the code list destroyed? How will reports will be written, in aggregate terms, or will individual responses be described? Will subjects be identified in reports (see item 5 on page 10)? Describe disposition of tapes/films at the end of the study. If tapes are to be kept, indicate for how long and describe future uses of tapes.

*Confidentiality will be preserved. All subjects will be given a laboratory identification number. There is a file that cross-lists names and ID numbers. The files will be integrated into the filing system of the Adult Fitness Program and will be kept as long as that program exists. All data will be logged and identified by identification numbers. No subject will be referred to by name in any publication or summary of this work. All data will be kept in locked PI's laboratory, the*

*Clinical Exercise Physiology of the Human Performance Laboratories in the Department of Kinesiology, School of HPER, and will be available to the investigators.*

G. What, if any, benefit is to be gained by the subject? In the event of monetary gain, include all payment arrangements (amount of payment and the proposed method of disbursement), including reimbursement of expenses. If class credit will be given, list the amount and the value as it relates to the total points needed for an A. List alternative ways to earn the same amount of credit. If merchandise or a service is given, indicate the value. Explain the amount of partial payment/class credit if the subject withdraws prior to completion of the study. (See policy at http://www.indiana.edu/~resrisk/compensation.html)

*The subject will receive a free evaluation of general health/fitness and exercise tolerance, including ECG, heart rate, and blood pressure responses. The same procedures perform independently at the IU Adult Fitness Program, which would result in costs of $200. If performed in clinical settings, reimbursement estimates are between $325.49 and $831.70. For participation in this study, a gift certificate ($20 worth) will be offered to each subject. After the completion of the whole study, $130 will be provided to subjects. The subject is free to withdraw prior to completion of the study. The results of all the testing will be sent to the subject and/or to the subject's primary physician if the subject wants. Patient evaluation and management by the primary physician may be enhanced with the use of 24-hour ambulatory blood pressure measurements. If desired, exercise counseling will be also provided.*

H. What information may accrue to science or society in general as a result of this work?

*The use of life style modifications or non-pharmacological treatments has been recommended for the treatment of hypertension due to economics, drug side effects, and low adherence to antihypertnesive medication. Exercise has been recognized as the most effective non-pharmacological treatments. Exercise reduces systolic blood pressure 6.2 to 9.9 mmHg and diastolic blood pressure 6.8 to 7.6 mmHg. However, not all hypertnesive adults participate in exercise program. The accumulation of short bouts of exercise may fit to the busy days, and promote prevention and treatment of hypertension.*

I. Coinvestigators, Cooperating Departments, Cooperating Institutions. If there are multiple investigators, please indicate only one person on the Documentation of Review and Approval (page 3) as the principal investigator; others should be designated as coinvestigators here. **Coinvestigators, not signing on page 3, should sign here, pledging to conform to the sentences on page 3.** If you anticipate that another department or institution may be involved in this research, list that here. If you are working with another institution, please include a letter of cooperation from that institution.
**Please provide the person's name and e-mail address.**

NONE

**INDIANA UNIVERSITY**
**BLOOMINGTON CAMPUS COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS**

## (((((((((((((( *STUDY AMENDMENT* ((((((((((((((

Study # 03-8515 of

Research Project Utilizing Human Subjects

**NOTE TO INVESTIGATORS: Study amendments may not be instituted until written approval from the IUB Campus Committee for the Protection of Human Subjects has been given. Return this form to: HSC, Caramichael Center L03, 530 E. Kirkwood Ave., IUB. Please complete in a legible manner! This entire page MUST be on a single sheet of paper. Use this as a cover page and attach pages with the information requested in items 1 and 2.**

TITLE OF PROJECT A comparison of a single exercise treatment to a physical activity treatment in hypertension and prehypertension

PRIN. INVESTIGATOR Saejong Park SCHOOL/DEPARTMENT HPER/Kinesiology

ADDRESS (campus or US) HPER 070 E-MAIL saejpark@indiana.edu TELEPHONE 812-855-7556

FUNDING AGENCY: American Heart Association

**********

**PLEASE USE THIS AS A COVER PAGE.**
**ATTACH PAGES with the INFORMATION REQUESTED in items 1 and 2.**

1. Describe the proposed change(s) and rationale for the change(s). Include any changes to project start and end dates. If submitting a revised questionnaire or survey, please include a copy **with** changes highlighted.
   See attachment.
2. Describe how the amendment will affect the risk:benefit ratio for subjects.
   The risk: benefit ratio for subject will not be affected by the amendment.
3. Does the proposed amendment require changes in the Consent Statement/Information Sheet? Yes
   If the answer is **yes**, check the appropriate line and attach a copy of the revised Consent Statement/Information Sheet, **with** changes highlighted.
   _____ The new Consent Statement/Information Sheet is in addition to the current one
   ___X__ The new Consent Statement/Information Sheet is to replace the current one.

Park, Saejong _____ _____ _____

Principal Investigator (typed/printed name) (signature—must be PI's own signature) (date)

Wallace, Janet P. _____ _____ _____

Faculty Advisor/Sponsor (typed/printed name) (signature—must be sponsor's own signature) (date)

**********

**CAMPUS LEVEL REVIEW**

_____ The Amendment of this protocol for use of human subjects has been reviewed and approved by the IUB Campus Committee for the Protection of Human Subjects.

_____ Exempt review ¶#_____ _____ Exempt review with documentation of consent ¶#_____

_____ Expedited review _____ Full Committee review

_____ _____
Chairperson/Agent IUB Committee Date

logged in ts _____ approval logged _____ copy to PI _____ notice to SOE _____
rank code _____
test: PI _____ sponsor _____ co-PI _____

10/03;www;msw

1. Describe the proposed change(s) and rationale for the change(s). Include any changes to project start and end dates. If submitting a revised questionnaire or survey, please include a copy **with** changes highlighted.

The proposed changes will be the duration of monitoring ambulatory EKG and physical acitiviy.

First, prehypertensive adults will be included in this study. In 2003, prehypertension is newly classified to promote lifestyle modifications to prevent cardiovascular disease. Prehypertension is defined as a systolic blood pressure of 120-139 mm Hg or a diastolic blood pressure of 80-89 mm Hg. The rational for this new classification is that prehypertensvie adults are at increased risk for progression to hypertension: those in the 130/80 to 139/89 mm Hg are at twice this risk to develop hypertension as those with lower values.

Second, subjects will be compensated according to the following scale: 1st lab test = $15, 2nd lab test = $35, 1st 24 Hour blood pressure monitor = $20, 2nd 24 Hour blood pressure monitor = $25, 3rd 24 Hour Blood Pressure monitor = $35. If subjects do not finish a particular session, subjects will still be paid the amount of money: If subjects complete the entire study, subjects will receive an additional $20 for a total of $150. This compensation has been approved by Human Subject Committee for original application.

Changes in the project start and end dates are 07/01/2004 and 06/30/2005.

## *NOTICE OF APPROVAL*

INDIANA UNIVERSITY

**NOTICE OF APPROVAL**
**CONTINUING REVIEW**
**FULL COMMITTEE REVIEW**

**TO:** Saejong Park
HPER

**DATE:** October 26, 2004

**FROM:** Cybil Cole, Director Human Subjects Risk Compliance

**RE:** Protocol entitled: Blood Pressure Reduction on Following the Accumulation of Short Bouts Versus One Long Bout of Exercise in Hypertension
Protocol #: 03- 8515

The Human Subjects Committee (HSC) has reviewed and approved the Continuing Review for the research protocol referenced above. As the principal investigator of this study you assume the following reporting responsibilities:

**CONTINUING REVIEW:** A status report must be filed with the committee. You are required to apply for renewal of approval at least once a year for as long as the study is active. All projects will automatically receive a renewal notice from the HSC. **This study is approved from October 21, 2004 to October 20, 2005.**

**AMENDMENTS:** Investigators are required to report on these forms **ANY** changes to the research study (such as design, procedures, consent forms, or subject population, including size). An amendment form is attached for your future use. ***The new procedure may not be initiated until HSC approval has been given.***

**AUDIT OR INSPECTION REPORTS:** Investigators are required to provide to the HSC a copy of any audit or inspection reports or findings issued to them by regulatory agencies, cooperative research groups, contract research organizations, the sponsor, or the funding agency.

**COMPLETION:** You are required to notify the HSC office when your study is completed (data analysis finished). Please contact the HSC office for the appropriate form to use.

**ADVERSE REACTIONS:** If any unexpected adverse reactions occur as a result of this study, you must notify the HSC office immediately. A written report must be filed within 3 working day.

**CONSENT FORMS:** All subjects should be given a copy of **the stamped approved** consent form. You must retain signed consent documents for at least three years past completion of the research activity.

We suggest you keep this letter with your copy of the approved protocol. Please refer to the exact project title and protocol number in any future correspondence with our office. All correspondence must be typed.

Enclosures: Continuing Review Approval
Amendment Form
Approved Consent Form- **stamped copy must be used**

Federal Wide Assurance #FWA00003544-IRB00000222
For additional FWA information, see the Web site at http://www.iupui.edu/~resgrad/spon/fwa.htm

OFFICE OF THE VICE PRESIDENT FOR RESEARCH

BLOOMINGTON CAMPUS COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS

Location:
Indiana University
Carmichael Center L03
530 East Kirkwood Avenue
Bloomington, Indiana

Mailing Address:
P.O. Box 1847
Bloomington, Indiana
47402

812-855-3067
Fax: 812-856-1535
E-mail:
iub_hsc@indiana.edu
WWW Address:
http://www.indiana.edu/
~resrisk.html

## *CONTINUING REVIEW OR TERMINATION REPORT*

FC

INDIANA UNIVERSITY
BLOOMINGTON CAMPUS COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS

RECEIVED
SEP 08 2004
HUMAN SUBJECTS COMMITTEE

**CONTINUING REVIEW or TERMINATION REPORT**
of
Research Project Utilizing Human Subjects

Study # 03-8515

**Federal regulations require that continuing reviews of all non-exempt activities be conducted at least annually. Therefore, this form must be completed and returned to the Human Subjects Committee, Carmichael Center L03, 530 E. Kirkwood Ave. IUB. If this study has been/will be terminated, or will not be done, it is still imperative that you complete and return this form, so that we can update our files accordingly. Please complete in a legible manner!**

TITLE OF PROJECT Blood pressure reduction on following the accumulation of short bouts versus one long bout of exercise in hypertension

PRIN. INVESTIGATOR _____ SCHOOL/DEPARTMENT HPER / Kinesiology

ADDRESS (campus or US) HPER 070, IUB E-MAIL _____ TELEPHONE 812-333-8249

1. Current status of research project: **(You must fill in this section. Note that continued HSC oversight is required if A or B is completed.)**

   A. Interaction/intervention with subjects:
   ____ Are being used: Date started: _____ Anticipated completion date: _____
   _V_ Will be used beginning: (date) 11-1-04 Anticipated completion date: 11-1-05

   B. Accessing identifiable data:
   _____ Study is ongoing for data analysis only. Anticipated completion of data analysis: _____

   C. Discontinue/Terminate:
   _____ Use of subjects was completed: (date) _____
   _____ Data analysis was completed: (date) _____
   _____ Study will not be done; close this file; explain: _____
   _____ Other; explain: _____

2. What is the funding status of the study? Indicate source, length of funding, and agency grant #.

3. How many subjects have completed the study, since the last report? NONE

4. How many subjects have completed the study, since the study started? NONE

5 **For NIH-sponsored studies, you must report the total number in the following categories (on site):**

| | American Indian or Alaskan Native | Asian or Pacific Islander | Black, not of Hispanic Origin | Hispanic | White, not of Hispanic Origin | Other or Unknown | Total |
|---|---|---|---|---|---|---|---|
| Female | | | | | | | |
| Male | | | | | | | |
| Unknown | | | | | | | |
| Total | | | | | | | |

6. Will more subjects be recruited? Yes If yes, how many? 20

7. Did any subjects withdraw from the study since the last report? NO If yes, state the number and reasons for withdrawal:

8. If no subjects are involved, explain why: funding pending

9. Were there any problems or complications in the study that affected the subject or others? No If yes, a description of any problems or complications must be provided.

10/03; wp

**COMPLETE NEXT PAGE ALSO.**

10. Describe any changes or deviations since last approval:

None

11. Has there been any change in the financial interests of anyone participating in the design, conduct, or reporting of this research that would affect the conflict of interest statement for this project since the last report? If yes, please explain.

No

12. Please provide the names and e-mail addresses of the current co-investigators on this project.

None

13. Provide a brief summary of progress and results.

None

14. **If this study is active and additional subjects will be recruited,** a copy of the current Informed Consent Statement **must** be returned with this form (even if it is the same as previously approved.) Any change to the original consent must be highlighted.

SIGNATURES:

| Principal Investigator (typed/printed name) | (signature–must be PI's own signature) | (date) |
|---|---|---|
| Faculty Advisor/Sponsor (typed/printed name) | (signature–must be sponsor's own signature) | (date) |

**CAMPUS LEVEL REVIEW**

_____ The continuing review of this **ongoing** protocol for use of human subjects has been reviewed and approved by the IUB Campus Committee for the Protection of Human Subjects for a one-year period beyond the approval date unless otherwise indicated.

_____ The closing report of this **terminated** protocol for use of human subjects has been reviewed and accepted by the IUB Campus Committee for the Protection of Human Subjects.

_____ Expedited Review _____ Full Committee Review

Chairperson/Agent IUB Committee _____ Date _____

logged in ts _____ approval logged _____ copy to PI _____

test: PI _____ sponsor _____ co-PI _____

4/03; wp

## *INDIANA UNIVERSITY – BLOOMINGTON*

## *INFORMED CONSENT STATEMENT*

**A comparison of a single exercise treatment to a physical activity treatment in hypertension and prehypertension**

You are invited to participate in a research study. This study will be conducted by a doctoral student under an authorized research program with the supervision of Janet P. Wallace, Ph.D. FASCM, and Larry Rink, M.D. at Indiana University. The purpose of this study is (1) to study how effective the accumulation of short bouts of brisk walking compared to one long bout of brisk walking is to reduce blood pressures (2) to observe the nature of the blood pressure reduction following each successive short bout of exercise, and (3) to investigate the role of nervous system as a possible mechanism for the blood pressure reduction following the brisk walking in adults with pre-high and high blood pressure.

**INFORMATION**

Design: You will be asked to have a physical examination at your expense and to have clearance from your primary physician to participate this study. You will be asked to report to the Clinical Exercise Physiology of the Human Performance Laboratories in the Department of Kinesiology, School of HPER for all the procedures in the study. You will complete two days of blood pressure screening. If your primary physician gives you permission to discontinue your medications for this study, your will have more blood pressure screenings after you stop taking your medications. You will complete two days of laboratory testing. Then, there will be two exercise and one control (without exercise) sessions. Each session will begin in the morning. The control session will be a day without exercise. On one of the exercise sessions you will walk on the treadmill for 40 minutes. On the other exercise day you will walk on the treadmill for four 10 minute sessions spread throughout the morning. On a control day and on days following exercise sessions, you will wear the ambulatory blood pressure and heartbeat (or EKG) monitor for 24 hours. The two exercise sessions will be greater than 7 days apart to avoid training effect. The order of the control and exercise treatments will be randomized. The total required time will be 10 to 11 hours over 21 to 30 day period. Approximately 20 hypertensive and 20 prehypertensive adults will be recruited for this study.

**Blood Pressure Screening**

Your blood pressure will be taken at least three times on two separate days. A blood pressure cuff will be attached to your upper arm, inflated, and released. This test will be repeated 3 times, and an average blood pressure be will be calculated. You will be classified to pre-high blood pressure or high blood pressure based on the screening blood pressure if your doctor did not confirm you have high blood pressure.

If you discontinue your blood pressure medication with your doctor's approval for this study, you will have more blood pressure screenings: every day for the first week and every other day for the rest of the study. You will be referred back to your primary physician to resume your medication and withdraw from the study if the screening blood pressures exceed the criterion blood pressure measurement (>3 days in a row) determined by your primary physician.

Subject's Initials

**Laboratory Testing**

*1. First Day of Testing: Quiet Testing (1-1.5 hours)*

_____ Fasting venous blood draw: You must be fasting for at least 12 hours prior to this test. A 20-45ml sample of venous blood will be drawn by a certified technician via sterile techniques for analysis of cholesterol, triglycerides, glucose, and various electrolytes and enzymes. This blood draw will take place at the University Health Center.

_____ 12-Lead Electrocardiogram (EKG): You will lie on a cot and have electrodes attached to your arms, legs, and chest to observe the electrical activity of your heart. You will also be asked to breathe deeply for 20 seconds to observe how deep breathing affects your EKG.

_____ Pulmonary Function Testing (For smokers only): You will breathe in and out as hard and fast as you can with room air through hoses attached to the computer to determine the capacity of your lung. This will be done for smokers to assure that lung function will not limit the ability to do exercise.

**Risks**

The risks associated with EKG and pulmonary function test are minimal. The risks associated with the venous blood draw may include soreness, bruising, fainting, and/or swelling at the puncture site. These risks are minimized by having the blood drawn by a trained technician at the Health Center while you are seated.

*2. Second Day of Testing: Exercise Testing (2 hours)*

_____ 12-Lead Electrocardiogram (EKG): Before the exercise test, you will lie on a cot and have electrodes attached to your shoulders, hips, and chest to observe the electrical activity of your heart. You will be also asked to stand up after recording an EKG in the lying position. Another EKG will be recorded in the upright position.

_____ Maximal Graded Exercise Test: This test is designed to measure your fitness and cardiovascular response to exercise. You will walk on a motor-driven treadmill with the grade increasing progressively until fatigue, breathlessness, chest discomfort, and/or any other symptoms which indicate to the technicians or yourself that you should stop exercise. Heart rate, EKG and blood pressure will be monitored through the test. Your expired gases will be also collected through mouthpiece either throughout the test or at the end of the test.

**Risks**

The discomforts involved with maximal graded exercise testing can include episodes of transient light headaches, chest discomfort, leg cramps, occasional irregular heart beats and abnormal blood pressure responses. The risk of heart attack, although rare (approximately 1 to 3 in 10,000), does exist.

Reasonable effort will be made to conduct the test in such a way as to minimize discomfort and risk. In the unlikely event of a heart related emergency we will call Bloomington Hospital Ambulance Service. The laboratory is equipped to respond to such situations and its personnel are trained to administer emergency care in the form of Basic Life Support. Advanced Cardiac Life Support will be provided by Bloomington Hospital

Subject's Initials

Ambulance Service. There is a one hour recovery period following maximal exercise testing during which you should not subject yourself to additional stress such as a very hot or very cold shower, smoking, heavy food intake, or other exercise.

**Exercise Treatments (40 minutes each)**

Exercise treatments will be the accumulation of four short bouts (10 minutes each separated by at least 50 minutes) and one long bout (40 minutes) of brisk walking. The first session of short bouts of exercise will be administered between 9am and 9:30am, the second session between 10am and 10:30am, and the third session between 11am and 11:30am and the last session between 12pm and 12:30pm. One long bout of exercise will be between 12pm and 1pm. Each exercise session you will walk on a motor driven treadmill at 50% of your exercise capacity, which will be estimated from your maximal graded exercise test. Expired gases will be measured during the 3$^{th}$ through the 4$^{th}$ minutes to confirm your exercise intensity. The work rate will be adjusted if it is not within $\pm$10% of your target exercise intensity. Expired gases will then be measured during the 6$^{th}$ through the 7$^{th}$ minutes to confirm the new exercise intensity. Heart rate (every minute) and blood pressure (every 2 to 5 minutes) will be measured during the exercise session.

**Risks**

The discomforts involved with exercise sessions can include episodes of transient light headaches, chest discomfort, leg cramps, occasional irregular heart beats and abnormal blood pressure responses. The risk of heart attack, although rare, is significantly reduced from exercise testing because of the sub-maximal intensity (approximately 1/300,000 man hours of exercise).

Reasonable effort will be made to minimize risk through the use of proper warm-up, exercise and cool-down technique. Mouth piece will be sanitized with proper detergents. In the unlikely event of a heart related emergency we will call the Bloomington Hospital Ambulance Service. The laboratory is equipped to respond to such situations and its personnel are trained to administer emergency care in the form of Basic Life Support. Advanced Cardiac Life Support will be provided by Bloomington Hospital Ambulance Service.

**Ambulatory Blood Pressure, Heartbeat (or EKG) and Activity Monitoring**

*1. On one day for successive short bout of exercise (4 to 5 hours)*

You will be asked to report the laboratory at between 8am and 8:30am and to stay at the lab until 12:30pm on one day for the accumulation of short bouts of exercise. Ambulatory blood pressure, heartbeat (or EKG) and activity monitors will be set up. Ambulatory blood pressure, EKG and activity monitors will be started following a 10-minute seated resting period. The Accutracker II will be used for all ambulatory blood pressure measurements. The sampling interval will be 5 minutes for 15 minutes prior to short bout of exercise. The cuff inflation for each measurement will be 30 mmHg greater than the previous reading. The cuff deflation will be set at 3 mmHg/second. The blood pressure monitor will be worn on the non-dominant arm. The Aria digital recorder will be used to record your heartbeat or EKG. Total seven (three from ambulatory blood pressure monitor and four from EKG monitor) EKG electrodes will be placed in chest. Electrode wires will be taped securely to the chest. The RT3 monitor (beeper size) will be attached to a belt at the hip of your dominant leg to monitor your activity.

Subject's Initials

During the short bout of exercise (10 minutes) and resting period you will wear ambulatory blood pressure, EKG monitors and activity monitor. During the long bout of exercise you only wear activity monitor. After the long bout of exercise, you will be attached to the ambulatory blood pressure and EKG monitors. The sampling interval of ambulatory blood pressure monitor will be 5 minutes for a 15 minutes and 15 minutes for a 50-minute supine resting period for the successive short bouts of exercise.

**2. On three days following the control and two exercise sessions (20 mins)**

Ambulatory blood pressure and heartbeat monitoring will be taken following the control and two exercise sessions. The sampling interval of the Accutracker II, will be randomized to take a reading on the average of every 15±5 minutes for a 12-hour collection period following two exercise and one control (without exercise) sessions. The monitor will be programmed to take no readings following the 12-hour collection period. You can take all the monitors off when you are awake. One repeat measurement will be taken if the first measurement was unsuccessful. The cuff inflation for each measurement will be 30 mmHg greater than the previous reading. The cuff deflation will be set at 3 mmHg/second. The blood pressure monitor will be worn on the non-dominant arm. EKG electrodes will be placed in chest. Electrode wires and blood pressure tubing will be taped securely to the chest. You will be given the option to secure the recording unit with a belt or the shoulder strap provided. A roll of micropore tape and extra electrodes will be given to re-tape areas or to replace electrodes if needed.

The Aria digital recorder will be used for 12-hour EKG recording. This is a device which records your heartbeat or EKG. Four EKG electrodes will be placed in chest. Electrode wires will be taped securely to the chest. You will be given the option to secure the recording unit with a belt or the shoulder strap provided. Extra electrodes will be given to replace electrodes when they become loosened. Instructions will be given on how to replace electrodes.

The RT3 monitor will be used for 12-hour activity recording. The RT3 is a size of beeper. The RT3 monitor will be firmly attached to a belt at the hip of your dominant leg.

You will be encouraged to participate in normal daily activities. You will be asked to document 1) time of sleep, 2) time at work, 3) time of meals, and 4) time at leisure activities. You will be instructed 1) not to get the monitor wet, 2) not to exercise, 3) not to take a shower, 4) not to use electric blanket, 5) not to operate a lawn mower, a vacuum cleaner or any equipment which would cause vibration, and 6) to relax and straighten out the arm during the blood pressure recording for the entire 12-hour period.

**Risks**

The discomforts involved with ambulatory blood pressure monitoring can include minor disturbance of daily tasks, tightness of blood pressure cuff, and skin irritation from the tape and/or sleep interruption. There are rare events which include cases of minute spots of bruising and slight discoloration of skin, irritation to the veins, swelling, and abrasions. The discomforts associated with the heartbeat or EKG monitoring are minimal. Redness and/or itchiness at the electrode sites may occur.

Reasonable effort will be made to minimize discomforts. Blood pressure cuff will be inflated just little above your previous blood pressure. Phone numbers of the investigators will be provided to you if they have any problems with the device during the course of the monitoring.

Subject's Initials

**EMERGENCY MEDICAL TREATMENT**

In the unlikely event of physical injury resulting from your participation in this research, emergency medical treatment will be provided at no cost to you. Be certain that you immediately notify the researcher if you are injured. If you require additional medical treatment you will be responsible for the cost. No other compensation will be provided if you are injured in this research. Be certain that you immediately notify the researcher if you are injured.

**BENEFITS**

You will receive a free evaluation of general health/fitness and exercise tolerance, including EKG, heart rate, and blood pressure responses as well as information regarding the effectiveness of exercise to reduce your blood pressure. The same procedures are performed independently at the IU Adult Fitness Program (cost is $250). If performed in clinical settings, reimbursement estimate is $325.49-$831.70. Your physician will also receive this information which may aid in management of your health/disease if you want. Exercise prescription and counseling will also be provided on your request.

**CONFIDENTIALITY**

Data or answers to questions will remain confidential with regard to your identity. You will be given an identification number. All data will be logged and identified by identification numbers. All data will be kept in the locked investigators' laboratory, the Clinical Exercise Physiology and will be only available to persons conducting the research. Results will be made available to your physician. No subject will be referred to by name in any publication or summary of this work.

**COMPENSATION**

You will be compensated according to the following scale: 1st lab test = $15, 2nd lab test = $35, 1st 24 Hour blood pressure monitor = $20, 2nd 24 Hour blood pressure monitor = $25, 3rd 24 Hour Blood Pressure monitor = $35. If you do not finish a particular session you will still be paid the amount of money: If you complete the entire study you will receive an additional $20 for a total of $150.

**CONTACT**

If you have questions at any time about the study or the procedures (or you experience adverse effects as a result of participating in this study) you may contact

| | | | |
|---|---|---|---|
| Saejong Park | HPER 070 | Indiana University, Bloomington, IN 47405 | 855-7556 |
| Dr. Wallace | HPER 112-G | Indiana University, Bloomington, IN 47405 | 855-6384 |
| Dr. Rink | HPER 070 | Indiana University, Bloomington, IN 47405 | 855-7556 |

If you feel you have not been treated according to the descriptions in this form, or your rights as a participant in research have been violated during the course of this project, you may contact the office for the Human Subjects Committee, Indiana University, Carmichael Center L03, 530 E. Kirkwood Ave., Bloomington, IN 47408, 812/855-3067, by e-mail at iub_hsc@indiana.edu.

Subject's Initials

**PARTICIPATION**

Your participation in this study is voluntary; you may refuse to participate without penalty. If you decide to participate, you may withdraw from the study at any time. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed on your request.

**CONSENT**

I have read this form and received a copy of it. I have had all my questions answered to my satisfaction. I agree to take part in this study.

Subject's signature_____Date _____

Investigator's signature_____Date _____

Consent form date: February 20, 2004

IRB Approved
Approval Date: OCT 2 1 2004
Expires: OCT 2 0 2005

## *APPENDIX F - FORMS/RECRUITMENT MATERIALS*

***PUBLIC SERVICE ANOUNCEMENT***

Indiana University Clinical Exercise Physiology Lab Seeks
Volunteers for Exercise and Blood Pressure Study

The Indiana University Clinical Exercise Physiology laboratory is currently seeking volunteers over 18 years old who have prehypertension (a systolic blood pressure of 120-140 mm Hg or a diastolic blood pressure of 80-89 mmHg). The purpose of the study is to see if the accumulation of four short brisk walking sessions (10-min) is as effective in lowering your blood pressure as one single long brisk walkingsession (40-min) is.

After the completion of this study, you will receive $150. Prior physician approval is required to participate.

For more information on this study contact Saejong Park (saejpark@indiana.edu) or Janet P. Wallace, Ph.D. (wallacej@indiana.edu) at the Clinical Exercise Physiology Laboratory, 812-855-7556.

***TELEPHONE SCRIPT***

**Accumulation of four short bouts of brisk walking on blood pressure reduction in prehypertension**

Saejong Park, M.S.

Thank you for your interest in this study. Our purpose is to see if the accumulation of four short bouts of brisk walking is as effective as one long bout of brisk walking in order to lower your blood pressure.

Are you interested?

If the answer is no: "Thank you. If you know of anyone who might be interested, please give them our phone number"

If the answer is yes:

Do you know your blood pressure? What is your blood pressure? Is your blood pressure between 120 and 140 for the top number or between 80-89 for the bottom number?

If the answer is no: "Thank you for your interest, but you do not qualify for the study. If you know of anyone who might be interested, please give them our phone number"

If the answer is no: "Your blood pressure will be screened on two separate days in the laboratory and you might not be qualified for the study based on the screening blood pressure."

If the answer is yes:

This requires walking on a treadmill three times in one day, 10 minuets each time spread throughout the morning. The blood pressure reduction will then be compared to walking on the treadmill for one 40 minute walk. We will also have a day that you do not do any exercise. For each of these three days, you will wear a blood pressure monitor that measures your blood pressure every 15 minutes for 12 hours. We will also measure your heartbeat or EKG during that time.

Are you still interested?

If the answer is no: "Thank you for your interest. If you know of anyone who might be interested, please give them our phone number"

If the answer is yes:
To be eligible for the study you must

have clearance from your primary physician
complete a health history form
complete some laboratory testing so that we can find out how much exercise is safe for you.

Are you still interested in the study?

If the answer is no: “Thank you for your interest. If you know of anyone who might be interested, please give them our phone number”

If the answer is yes:

Once your physician gives permission, you will be scheduled for laboratory testing. This testing includes blood draw at IU health center, resting EKG, stress test, and lung function test (only for smokers). On the day of your stress test, you will walk on the treadmill until you cannot walk any longer. Your blood pressure, heart rhythm, signs and symptoms will be monitored by a physician and lab technicians.

After your treadmill test, you will be scheduled to return to the lab within a week to perform a 40-minute brisk walking and four 10-minute brisk walking on treadmill. The order of these will be randomized.

After each brisk walking on treadmill session you will wear 12-hour ambulatory blood pressure and heartbeat or EKG monitors (70 minutes). You will be asked to report to the lab and to wear 12-hour ambulatory blood pressure and EKG monitors on a day without exercise (20 minutes).

***PHYSICIAN LETTER***

February 16, 2004

Dear Physician,

A doctoral student in the Indiana University Clinical Exercise Physiology is currently conducting a research study to compare the blood pressure reduction following the accumulating four short bouts (10-minute) of brisk walking to the blood pressure reduction following one single long bout (40-minute) of brisk walking in prehypertensive adults. In 2003, prehypertension (defined as systolic 120-139 mm Hg or diastolic blood pressure 80-89mm Hg) is newly classified by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure to prevent cardiovascular diseases through health-promoting lifestyle modifications. Changes in autonomic nerve modulation measured by heart rate variability using the Holter monitor will be investigated as possible mechanisms of the blood pressure reduction following exercise interventions in hypertension.

Your assistance will be needed if any of your patients want to participate in the study. Before entering the study, each participant must consult his/her physician for a physical examination.

A recruitment flyer on the study has also been enclosed if you would like to post it for your patients to read. Reports of the exercise testing and ambulatory blood pressure monitoring, and other reports requested on your patient will be sent to you.

Your assistance in the study is greatly appreciated. It is hoped that participating in this study will provide each participant a greater awareness of his/her personal fitness, health behaviors, and hypertensive disease. It is also hoped that the results of this study will promote a better understanding of how exercise intervention may assist in the management of prehypertension. If you have any questions, concerns, or comments, please contact the program at 855-7556.

Sincerely,

Saejong Park, Doctoral Student, Clinical Exercise Physiology
Janet P. Wallace, Ph.D., Research Director, Adult Fitness Program
Larry Rink, MD, Medical Director, Adult Fitness Program

## *PHYSICAL EXAMINATION AND MEDICAL HISTORY*

Name of Patient_____ DOB_____

## Medical History

| Does the above patient have or ever had the following conditions? (Please check the appropriate column). | No | Yes | Comments |
|---|---|---|---|
| Acute myocardial infarction | | | |
| Angina (please comment) | | | |
| Angina (please comment) | | | |
| Manifest circulatory insufficiency (CHF) | | | |
| Cardiomyopathy (IHSS) or Valvular heart disease (specify) | | | |
| Suspected or known aneurysm | | | |
| Embolism or thrombophlebitis | | | |
| ECG abnormalities (specify type) | | | |
| Active or suspected myocarditis or pericarditis | | | |
| Serious systemic disorder (ie: Mononucleosis, Hepatitis) | | | |
| Pulmonary disorders (ie: COPD, asthma, hypertension) | | | |
| Diabetes (specify type and severity) | | | |
| Uncontrolled metabolic disease (ie: Myxedema, Thyrotoxicosis) | | | |
| Electrolyte abnormalities (specify type) | | | |
| Prescribed medications (specify type) | | | |
| Neuromuscular, musculoskeletal, or rheumatoid disorders which would make exercise difficult | | | |
| Significant emotional distress | | | |

## Physical Examination

**Blood Pressure_____mmHg**

**Heart Sounds** (please check if present):

Lifts_____ Heaves_____ Clicks_____ Thrills_____ Murmurs_____(location and grade)

**Lung Sounds** (please describe auscultation):

Clear_____ Wheezes_____ Rales_____

**Quality of peripheral pulses** (please check):

Absent_____ 1/4_____ 2/4_____ 3/4_____ 4/4_____

**Edema** (please quantify if present):_____

| **Edema** (please quantify if present):_____<br>**Is this person capable of performing a maximal_____or moderate_____graded treadmill/bicycle exercise test?**<br>***If no, please comment.**_____ | **Yes** | **No** |
|---|---|---|
| **This individual is capable of participating in a maximal_____or moderate_____exercise program under the guidance of a certified exercise specialist.** | | |

Date of Health Examination_____ (must be valid within the past six month)

Signed_____ M.D._____

Date_____

(signature of physician) (printed name of physician)

Indiana University Adult Fitness Program (812) 855-7556

## *MEDICAL HISTORY/HEALTH HABIT QUESTIONNAIRE*

INDIANA UNIVERSITY
Adult Fitness Program

# Medical History/Health Habit Questionnaire

Name_____ Age_____ Birthdate_____
(Please print) Day/Month/Year

Work Address_____ Zip_____

Home Address_____ Zip_____

Work Phone_____ Home Phone _____ e-mail_____

1. LIST HOSPITALIZATION HISTORY

| Age at Hospitalization | Reason for Hospitalization | Duration of Stay | Comments |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

2. LIST CHILDHOOD DISEASES

Disease Age

_____
_____
_____

3. LIST ALL MEDICATIONS PRESENTLY TAKING

| Medication | Purpose | Dose | How Often |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |

4. FAMILY HISTORY OF HEART DISEASE/STROKE
Indicate immediate family members (parents, siblings, aunt, uncles) who have diagnosed heart disease/stroke and/or who have died from heart disease/stroke.

| Relationship | Type of Disease | Age at Diagnosis | Age at Death |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |

5. HIGH BLOOD PRESSURE
   a. Have you ever been told you have high blood pressure? _____Yes _____No
   b. If so, when?_____
   c. Was any treatment recommended? _____Yes _____No
   d. If so, what?_____
   e. Are you still undergoing that treatment? _____Yes _____No
   f. If no, when did yo stop?_____
   g. List any family members who have/had had high blood pressure:

| Relationship | Age at Diagnosis |
|---|---|
| | |
| | |
| | |
| | |

6. DIABETES
   a. Have you ever been told you have diabetes? _____Yes _____No
   b. If so, when?_____
   c. What type of treatment was recommended?
      Diet_____
      Insulin_____ Dose_____ Type if Insulin_____
   d. Are you still undergoing treatment? _____Yes _____No
   e. If no, when did you stop?_____
   f. List any family members who have/have had diabetes:

| Relationship | Type of Disease* | Age at Diagnosis |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

*Type I (▼insulin)
Type II (▲insulin)

7. a. Have you ever experienced chest discomfort? _____Yes _____No
   b. If so, when?_____
   a. Describe the nature of the discomfort._____
   b. What were you doing at the time?_____
   c. When does it disappear?_____
   d. Was medical advice sought? _____Yes _____No
   e. What type of evaluation was performed?_____
   f. What was the result/conclusion of this evaluation?_____
   i. Are you on any medication for chest discomfort? _____Yes _____No
   j. If so, what?_____ How Often?_____
   k. How much?_____

8. a. Have you ever experienced skipped heart beats, rapid heart rates or other arrythmias?_____Yes _____No
   b. If so, when?_____
   c. What?_____
   d. Was medical advice sought? _____Yes _____No
   e. What type of evaluation was performed?_____
   f. What was the result/conclusion of this evaluation?_____
   g. Are you on any medication as a result of this evaluation? _____Yes _____No
   h. If so, what?_____
   i. How often?_____
   j. How much?_____

9. a. Do you have any muscle or skeletal problem? _____Yes _____No
   b. What?_____
   c. Does this limit your ability to exercise? _____Yes _____No
   d. Has medical advice been sought? _____Yes _____No
   e. What was the conclusion of this medical evaluation_____
   _____
   f. Have you ever had any muscle or skeletal problems in the past? _____Yes _____No
   g. What?_____
   h. Was medical advice sought? _____Yes _____No
   i. What was the conclusion of this medical examination?_____
   _____

10. a. Are you presently engaging in any type of physical activity? _____Yes _____No

| Type of Exercise | How Long (min.) | How Often (days/week) | How Hard (Light-Moderate-Hard) | When Did You Start |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |

   b. Have you engaged in any type of physical activity in the past? _____Yes _____No

| Type of Exercise | How Long (min.) | How Often (days/week) | How Hard (Light-Moderate-Hard) | When Did You Start | When Did You Quit | Why |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

   c. Occupation_____ Years at present work status_____
   d. If retired, what was your occupation?_____
   e. Do you consider your day: _____Sedentary? _____Moderately active? _____Heavy work?
   f. How many hours do you spend sitting each day?_____

11. How many hours do you sleep a night?_____ Soundness of sleep:_____

12. a. Do you consider your day stressful? _____Yes _____No
   b. What is the nature of your stress?_____
   _____
   c. How do you handle your stress?_____
   _____

13. Which meals do you eat?

| | Daily | Occasionally | Never |
|---|---|---|---|
| Breakfast | | | |
| Early morning snack | | | |
| Lunch | | | |
| Afternoon snack | | | |
| Dinner | | | |
| Bedtime snack | | | |

14. a. Do you consider yourself overweight? _____Yes _____No
b. How long have you been overweight?_____
c. How many pounds would you like to lose?_____
a. Do you smoke? _____Yes _____No
b. What do you smoke?_____
c. How much?_____
d. Have you ever smoked in the past? _____Yes _____No
e. What did you smoke?_____
f. How many years?_____
g. How much?_____
h. When did you stop?_____
i. Why?_____

16. a. Do you drink alcohol? ____Yes _____No
b. What kind?_____
c. How often?_____
d. Did you ever use alcohol in the past? _____Yes _____No
e. What?_____
f. How much? How often?_____
g. How many years?_____ When did you start?_____

17. a. List any known allergies._____

Any additional pertinent information_____

_____

_____

Signature_____ Date_____

*OFFICE USE ONLY*

Type of Membership_____
Group_____

Interviewer Comments_____

_____

_____

**Interviewer**_____ **Date**_____

ADULT FITNESS PROGRAM

## *EXERCISE TEST DATA SHEET*

Time_____ a.m.

I.D.#_____Name_____Date_____ Age___ Sex____
Last First Day Month Year
DOB _____ Weight _____ lb. _____ kg. Physician _____
Fasting: Yes_____ No_____ Do you smoke: Yes_____ No_____
Rest BP (mm Hg) #1_____/_____-_____ #2 _____/_____-_____ #3_____/_____-_____
Height _____in. _____ cm. Rest HR _____ b/min. Time of Day _____

Recent illness, Chest Discomfort, or Arrhythmias, etc.
_____
_____

Current Medications
_____
_____

Rest EKG_____ Axis_____* P-R _____ sec.

MD comments/Conclusions_____
_____**X**_____

Previous test :

| Date | Speed | Final grade | Time | Peak HR | Peak $VO_2$ | EKG |
|---|---|---|---|---|---|---|
| | | | | | | |

| Time (min) | Grade (%) Load (rpm) | Rate (mph) (kpm/min) | Work Rate (kpm/min) | Heart Rate (beats/min) | Ectopy | Blood Pressure mmHg Phase: 1/4-5 | RPE | Comments |
|---|---|---|---|---|---|---|---|---|
| baseline | | | | | | / | | |
| 0-1 | | | | | | / | | |
| 1-2 | | | | | | / | | |
| 2-3 | | | | | | / | | |
| 3-4 | | | | | | / | | |
| 4-5 | | | | | | / | | |
| 5-6 | | | | | | / | | |
| 6-7 | | | | | | / | | |
| | | | | | | / | | |
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| peak | | | | | | / | | |
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| | | | | | | / | | |
| | | | | | | / | | |

Reason for termination_____

***BLOOD PRESSURE SCREENING***

Name: _____ Subject ID: _____

DATE: _____
**Right Arm**

| | Systolic blood pressure | Diastolic blood pressure |
|---|---|---|
| 1st trial | | |
| 2nd trial | | |
| 3rd trial | | |

DATE: _____
**Left Arm**

| | Systolic blood pressure | Diastolic blood pressure |
|---|---|---|
| 1st trial | | |
| 2nd trial | | |
| 3rd trial | | |

DATE: _____
**Right / Left** Arm

| | Systolic blood pressure | Diastolic blood pressure |
|---|---|---|
| 1st trial | | |
| 2nd trial | | |
| 3rd trial | | |

*AVERAGE BLOOD PRESSUE: _____ mm Hg

* average blood pressure is calculated based on blood pressures of both visits using **Right / Left** arm.

***GXT RESULT LETTER***

Subject Name
Address

Dear Subject,

This is a summary of the laboratory evaluation for you conducted on Month Year by the Clinical Exercise Physiology Program.

**RESTING VARIABLES:**

The resting heart rate was 79 beats per minute. Resting blood pressure, using first and fourth sounds of Korotkoff, was xxx / xx mm Hg (a mean of six measurements over two days). Resting electrocardiogram demonstrated - _____. Fasting blood chemistries measured on Month Year, demonstrated a serum glucose of xx mg/dL, a total cholesterol of xxx mg/dL, and a HDL of xx mg/dL, and a LDL of xxx mg/dL as well as a serum triglycerides of xxx mg/dL.

**EXERCISE TESTING:**

A graded exercise test was performed on a motor driven treadmill. The workrate began at x mph and x % grade. Incremental work was performed until a maximal workrate was achieved at xx:xx minutes. The maximal voluntary effort was reached at x mph and x % grade. The test was terminated due to - _____. The highest heart rate achieved was 181 beats per minute. Heart rate response to exercise and recovery was _____. ECG showed _____ at rest and during submaximal exercise. Blood pressure response to exercise was _____ although blood pressure response during recovery was normal. Expired gases were collected during this test. Measured peak oxygen uptake ($VO_{2peak}$) for this test was xx $ml \cdot kg^{-1} \cdot min^{-1}$. Your predicted $VO_{2max}$ was xx $ml \cdot kg^{-1} \cdot min^{-1}$. The conclusion of Dr. Hipskind, physician in attendance, _____.

**RECOMMENDATIONS**

The exercise prescription based on the goal of your blood pressure reduction includes 3-7 days/week of walking for 30-60minutes at the exercise intensity of 40-70 %.

If you have any further questions about this test or our program please call 855-7556. Office hours are Tuesday and Thursday morning 8:00 am to 12:00 noon.

Thank you very much for your participation.

Sincerely,

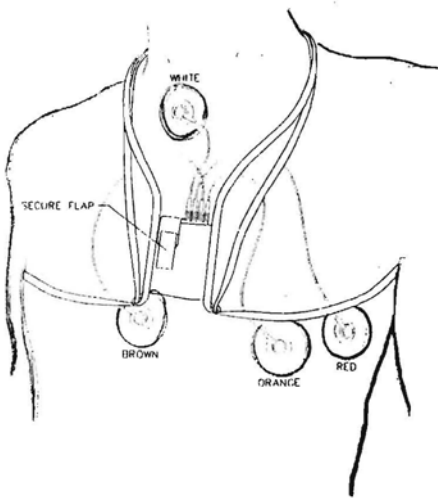
Saejong Park
Clinical Exercise Physiology

*INFORMATION FORM*

# AMBULATORY BLOOD PRESSURE AND EKG MONITORING

Thank you for volunteering for this research study. The purpose of this study is to see if the accumulation of four short bouts of brisk walking is as effective as one long bout of brisk walking in lowering your blood pressure. The following is a list of rules to follow when you wear the ambulatory blood pressure and EKG monitors.

1. Do not get the ambulatory blood pressure and EKG monitors wet.
2. Do not exercise or take a shower when wearing the blood pressure and EKG monitors.
3. Do not use an electric blanket.
4. Do not operate a lawn mower, a vacuum cleaner or any equipment which could cause vibration.
5. Replace electrodes with new electrodes when electrodes become loose as shown.



6. Relax your arm while the blood pressure cuff is pumping up.
7. The blood pressure monitor is programmed to take a blood pressure about every 15 minutes from 12pm to 2am. It will not take your blood pressure exactly every 15 minutes.
8. The blood pressure monitor is also programmed to inflate the cuff just a little above the last reading. The cuff should not pump up as high the first time each reading.
9. Please, record the following information.

| ***Time on Blood Pressure Monitor*** | ***Predominant Activity*** | ***Duration*** |
|---|---|---|
| | Sleep | |
| | Work | |
| | Meals | |
| | Leisure | |
| | | |
| | | |

Call us any time of day or night if the blood pressure monitor pumps up as high as it can go and/or if it pumps up every 5 to 7 minutes for an hour. We may come out and adjust it or we may ask you to turn it off.

| | |
|---|---|
| AFP Office | 855-7556 |
| Saejong Park | 333-8249 |
| Dr. Wallace | 334-8217 |

***SHORT BOUTS OF EXERCISE TREATMENTS***

Name: _____ Subject ID: _____ Date: _____

Age: _____ Sex: _____ Height (cm): _____ Weight (kg):_____

$VO_{2peak}$ (ml/kg/min): _____ $HR_{peak}$ (bpm): _____
Treadmill Speed (mph): _____ Treadmill Grade (%): _____

Target $VO_{2peak}$ by graph: _____ HR: _____
Treadmill Speed (mph): _____ Treadmill Grade (%): _____

Time at End of Exercise Treatment: _____
Time @ 24hr BP Monitor: _____
Test Operator: _____

| Stage | Time (min) | Time at BP Monitor | Speed (mph) | Grade (%) | HR (bpm) | | *BP* (mm Hg) | $VO_2$ (ml/kg/ min) | R P E |
|---|---|---|---|---|---|---|---|---|---|
| Rest | 0-5 | | | | | | | | |
| | 5-10 | | | | | | | | |
| | 10-15 | | | | | | | | |
| 1 | 0-2 | | | | | | | | |
| | 2-4 | | | | | | | | |
| | 4-6 | | | | | | | | |
| | 6-8 | | | | | | | | |
| | 8-10 | | | | | | | | |
| Recovery | 5 | | | | | | | | |
| | 10 | | | | | | | | |
| | 15 | | | | | | | | |
| | 20 | | | | | | | | |
| | 30 | | | | | | | | |
| | 40 | | | | | | | | |
| | 50 | | | | | | | | |
| 2 | 0-2 | | | | | | | | |
| | 2-4 | | | | | | | | |
| | 4-6 | | | | | | | | |
| | 6-8 | | | | | | | | |
| | 8-10 | | | | | | | | |
| Recovery | 5 | | | | | | | | |
| | 10 | | | | | | | | |
| | 15 | | | | | | | | |
| | 20 | | | | | | | | |
| | 30 | | | | | | | | |
| | 40 | | | | | | | | |
| | 50 | | | | | | | | |
| 3 | 0-2 | | | | | | | | |
| | 2-4 | | | | | | | | |
| | 4-6 | | | | | | | | |
| | 6-8 | | | | | | | | |
| | 8-10 | | | | | | | | |
| Recovery | 5 | | | | | | | | |
| | 10 | | | | | | | | |
| | 15 | | | | | | | | |
| | 20 | | | | | | | | |
| | 30 | | | | | | | | |
| | 40 | | | | | | | | |
| | 50 | | | | | | | | |
| 4 | 0-2 | | | | | | | | |
| | 2-4 | | | | | | | | |
| | 4-6 | | | | | | | | |
| | 6-8 | | | | | | | | |
| | 8-10 | | | | | | | | |

## *LONG BOUT OF EXERCISE TREATMENTS*

Name: _____ Subject ID: _____ Date: _____

Age: _____ Sex: _____ Height (cm): _____ Weight (kg):_____

$VO_{2peak}$ (ml/kg/min): _____ $HR_{peak}$ (bpm): _____
Treadmill Speed (mph): _____ Treadmill Grade (%): _____

Target $VO_{2peak}$ by graph: _____ HR: _____
Treadmill Speed (mph): _____ Treadmill Grade (%): _____

| Stage | Time (min) | Speed (mph) | Grade (%) | HR (bpm) | | BP (mm Hg) | $VO_2$ (ml/kg/ min) | RPE |
|---|---|---|---|---|---|---|---|---|
| 1 | 0-2 | | | | | | | |
| | 2-4 | | | | | | | |
| | 4-6 | | | | | | | |
| | 6-8 | | | | | | | |
| | 8-10 | | | | | | | |
| 2 | 0-2 | | | | | | | |
| | 2-4 | | | | | | | |
| | 4-6 | | | | | | | |
| | 6-8 | | | | | | | |
| | 8-10 | | | | | | | |
| 3 | 0-2 | | | | | | | |
| | 2-4 | | | | | | | |
| | 4-6 | | | | | | | |
| | 6-8 | | | | | | | |
| | 8-10 | | | | | | | |
| 4 | 0-2 | | | | | | | |
| | 2-4 | | | | | | | |
| | 4-6 | | | | | | | |
| | 6-8 | | | | | | | |
| | 8-10 | | | | | | | |

Time at the End of Exercise Treatment: _____
Time @ 24hr BP Monitor: _____
Test Operator: _____

***BLOOD PRESSURE RESULT LETTER***

Clinical Exercise Physiology
Indiana University

## Blood Pressure and Exercise Study

You, _____, participated in a research study entitled a comparison of a single exercise treatment to a physical activity treatment in prehypertension at the Indiana University Clinical Exercise Physiology Program. The purpose of this research is to study how effective the accumulation of short bouts of brisk walking compared to one long bout of brisk walking is to reduce blood pressure, and to observe the nature of the blood pressure reduction following each successive short bout of exercise in prehypertension.

**Ambulatory Blood Pressure Results**

Here are the results of the 12-hour blood pressure monitoring for the exercise sessions (one long & four short bouts of brisk walking) and the control day (without exercise). The average blood pressure for the entire 12-hour period following exercise sessions is calculated (Mean 12-hr).

Table 1. 12-hour average blood pressure following exercise sessions and control session

| | Mean 12-hr SBP (mmHg) | Mean 12-hr DBP (mmHg) | Mean difference in 12-hr SBP/DBP (mmHg) |
|---|---|---|---|
| Control (without exercise) | | | |
| 40-min Exercise | | | |
| Accumulation of four 10-min Exercise | | | |

SBP: systolic blood pressure/DBP: diastolic blood pressure (mmHg)

Table 2. 50-minute average blood pressure following each 10-minute of exercise

| | Mean 50-min SBP (mmHg) | Mean 50-min DBP (mmHg) | Mean difference in 50-min BP/DBP (mmHg) |
|---|---|---|---|
| Baseline | | | |
| 1st | | | |
| 2nd | | | |
| 3rd | | | |

Saejong Park
Blood Pressure Study/Adult Fitness Program
HPER 070
Indiana University Bloomington, IN 47405

## *APPENDIX G - PAST RELEVANT PUBLICATION*

## *TIME OF DAY FOR EXERCISE ON BLOOD PRESSURE REDUCTION IN DIPPING AND NONDIPPING HYPERTENSION*

Journal of Human Hypertension (2005) 19, 597–605

www.nature.com/jhh

ORIGINAL ARTICLE

# Time of day for exercise on blood pressure reduction in dipping and nondipping hypertension

S Park, CA Jastremski and JP Wallace
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**Time of day (TOD) for exercise may influence blood pressure (BP) reduction in hypertension because of the diurnal variation of BP and the duration of BP reduction following a single bout of exercise. The purpose of this study was to observe the effects of TOD for exercise on ambulatory blood pressure reduction in dipping ($n=5$) and nondipping ($n=9$) hypertension (<10% drop in nighttime BP ($BP_{night}$)). Hypotheses: (1) evening exercise ($PM_{ex}$) would exhibit a greater $BP_{night}$ reduction in Non-Dippers than Dippers, (2) morning exercise ($AM_{ex}$) would exhibit similar daytime BP ($BP_{day}$) reduction in Dippers and Non-Dippers, (3) $AM_{ex}$ would exhibit greater 24 h BP ($BP_{24h}$) reduction than $PM_{ex}$ in Dippers, and (4) $AM_{ex}$ and $PM_{ex}$ would exhibit similar $BP_{24h}$ reduction in Non-Dippers. BP responses to $AM_{ex}$ (0600–0800 h; 30 min at 50% $VO_{2peak}$) and $PM_{ex}$ (1700–1900 h) were compared to each control day in a randomized design. Systolic (S) and diastolic (D) BP were averaged for $BP_{24h}$, $BP_{day}$, and $BP_{night}$. A two-way ANOVA (dipping X time of exercise) using BP reduction with repeated measures were performed at $P<0.05$. Findings: (1) Non-Dippers respond to exercise despite of TOD for exercise, (2) $PM_{ex}$ exhibited a greater $SBP_{night}$ reduction in Non-Dippers than Dippers, (3) $AM_{ex}$ exhibited similar $SBP_{day}$ reductions in Dippers and Non-Dippers, and (4) $AM_{ex}$ and $PM_{ex}$ exhibited similar $SBP_{24h}$ reduction in Dippers and Non-Dippers. Dippers and Non-Dippers respond differently to TOD for exercise. The duration of the BP reduction persists up to 24 h after exercise.**
*Journal of Human Hypertension* (2005) **19,** 597–605.
doi:10.1038/sj.jhh.1001901; published online 16 June 2005

**Keywords:** diurnal variation; circadian rhythm; ambulatory blood pressure; post-exercise hypotension; physical activity

## Introduction

Hypertension, a major modifiable risk factor for stroke,[1] coronary artery disease,[1] congestive heart failure,[2] and end-stage renal disease,[3] is the most common primary diagnosis in the US. Healthy lifestyle modification, including physical activity and exercise, is recommended as the initial treatment option to control hypertension.[4–7]

Even though endurance exercise training lowers blood pressures in hypertensive patients,[8–10] approximately 25% of the hypertensive patients do not exhibit blood pressure reduction associated with exercise training.[8] Hypertensive patients who do not exhibit nocturnal dipping (Non-Dippers: defined as <10% reduction in average nighttime blood pressure compared to average daytime blood pressure)[11] have been identified among the non-responders to exercise training.[12] Nami *et al*[12] reported that aerobic exercise training failed to reduce blood pressure in Non-Dippers while it did reduce blood pressure in hypertensive patients who exhibited nocturnal dipping (Dippers). The unresponsiveness of the Non-Dippers to exercise treatment could not be attributed to salt intake and other metabolic factors.[12] Non-dipping hypertension is associated with a higher degree of cardiovascular complications and more serious end-organ damage than Dipping hypertension.[11] Thus, a more effective exercise programme for Non-Dippers may be warranted.

The reduction in blood pressure following a single bout of exercise has been reported to persist for up to 11–12 h under free-living conditions for systolic blood pressure (5–8 mmHg) and/or up to 4–8 h for diastolic blood pressure (6–8 mmHg).[13–17] Presenting an exercise treatment prior to the period of highest blood pressure elevation may result in a more attenuated response because greater blood pressure reductions can be found in higher pressures.[18] Given this fact, morning exercise may be more effective in

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reducing the elevated daytime pressures in dipping and nondipping hypertension whereas evening exercise may be more effective in reducing the elevated nighttime pressures in nondipping hypertension. Thus, the study of the time of day (TOD) for exercise may be a conceptual approach for a more individualized exercise prescription in nondipping hypertension.

The purpose of this study was to observe the effects of the TOD for exercise on the reduction of ambulatory blood pressure in dipping and nondipping hypertension. It was hypothesized that (1) evening exercise would exhibit a greater reduction in nighttime blood pressure in nondipping hypertension than in dipping hypertension, (2) morning exercise would exhibit a similar daytime blood pressure reduction in dipping and non-dipping hypertension, (3) morning exercise would exhibit greater 24 h blood pressure reduction in dipping hypertension than evening exercise, and (4) morning and evening exercise would exhibit similar reductions in 24 h blood pressure in nondipping hypertension.

## Materials and methods

Procedures included (1) blood pressure screening, (2) maximal graded exercise testing, and (3) four 24 h ambulatory blood pressure monitoring trials following: (a) morning and evening exercise treatments (30 min walk at 50% of the peak oxygen uptake or $VO_{2peak}$), and (b) the corresponding morning and evening control treatments. The first level of randomization was the TOD. The second level of randomization was the order of exercise and control within the corresponding TOD treatment. All procedures were approved by the Committee for protection of Human Subjects at Indiana University. Written informed consent was obtained prior to participation.

### Subjects

Hypertensive middle-aged adults were recruited for this study. Hypertensive subjects were defined by one of the following: (1) having had a previous diagnosis of hypertension by a primary physician; (2) having a mean screening systolic blood pressure $\geqslant$ 140 mmHg and/or a mean diastolic blood pressure $\geqslant$ 90 mmHg taken from at least two readings on two days, three days apart;[19] or (3) exhibiting a mean daytime ambulatory blood pressure of $\geqslant$135/85 mmHg.[5] To be classified as Dippers or Non-Dippers, the subject had to exhibit the nocturnal blood pressure pattern on both control treatments. Non-Dippers were defined as hypertensive adults who exhibited <10% decrease in average nighttime systolic blood pressure compared to average daytime blood pressure. Dippers were defined as $\geqslant$10% decrease in average nighttime systolic blood pressure. Subject exclusion criteria included (1) significant cardiovascular or renal disease, (2) significant dysrhythmia, (3) brachial artery bruits, (4) cardiac or renal transplant patients, and (5) treatment with antihypertensive medications. A physician clearance by the subject's primary physician was required for every subject prior to participation in the study. With approval of their primary physician, hypertensive subjects who were taking antihypertensive medications discontinued the medications 2 weeks prior to maximal graded exercise test. Antihypertensive medications were discontinued for the duration of the study which was approximately 4–5 weeks. Blood pressures were closely monitored during this withdrawal period.

### Blood pressure screening

For all subjects, three blood pressure measurements were taken by auscultation on two separate days, three days apart (a total of six measurements). On the first day, blood pressure measurements were taken in both arms. The arm with the highest blood pressure was used for both screening periods. The screening blood pressure was an average of six measurements. Ambulatory blood pressure monitoring was also conducted to confirm high blood pressure in selected subjects who did not meet the clinical screening criteria.

### Maximal graded exercise test

The graded exercise test began between 2.5 and 4.0 mph at 0% grade. The speed remained constant while the grade increased 1.0% every minute until a maximal voluntary effort was achieved or limited by symptoms.[15,20] Blood pressure (by auscultation) and heart rate (by electrocardiogram) were measured every minute. $VO_{2peak}$ was obtained by on-line breath-by-breath using a Sensor Medics 2900 metabolic cart during the symptom-limited graded exercise test.

### Exercise treatment

Morning and evening exercise treatments were conducted between 0600 and 0800 h and between 1700 and 1900 h respectively. The exercise stimulus was a 30 min walk on a motor driven treadmill at 50% of $VO_{2peak}$. Each exercise treatment consisted of three sets of alternating 10 min exercise and 3 min rest period. Oxygen uptake ($VO_2$) was measured during the 7th–10th minutes of the first set of exercise to confirm the exercise intensity. The speed and/or grade of the treadmill was adjusted if it was not within $\pm$10% of the target $VO_2$. $VO_2$ was then measured during the 7th–10th minutes of the next work interval to confirm the new exercise intensity. Heart rate was measured every minute and blood

pressure was measured every 2–5 min during the exercise.

### Nonexercise control treatment

Morning and evening control treatments were conducted between 0600 and 0800 h and between 1700 and 1900 h, respectively. The control treatments were defined as nonexercise treatments beginning at the same TOD corresponding to each exercise treatment. The subject reported to the lab approximately 15 min before the time when the ambulatory blood pressure monitor would have been activated for the exercise treatments. Control data were collected for the same time period as for the exercise treatments. No sham rest period was used for the control treatments to simulate the time of attention given to the subject during the exercise treatments because rest is considered as an intervention itself.

### Twenty-four hour ambulatory blood pressure monitoring

A total of four ambulatory blood pressure monitoring sessions were performed; two beginning in the morning (0700–0900 h) and two beginning in the evening (1700–1900 h). The respective control and exercise treatments were no further apart than four days for each subject, however, the two exercise treatments were greater than seven days apart to avoid a training effect.

The Accutracker II (SunTech Medical Instruments, Inc., Morrisville, NC, USA) was used for ambulatory blood pressure measurements. The sampling interval was randomized to take a reading on the average of every $15 \pm 5$ min for daytime hours (0600–2200 h) and on the average of every $30 \pm 5$ min for nighttime hours (2200–0600 h).[21] One repeat measurement was taken if the first measurement was unsuccessful during the daytime hours and two repeat measurements were taken during the nighttime hours. The inflation of the cuff for each measurement was programmed to inflate 30 mmHg greater than the previous reading. The cuff deflation rate was programmed at 3 mmHg/s. Subjects were asked to document time of sleeping. Subjects were asked to go to bed between 2000 and 2400 h and get up between 0600 and 1000 h. Subjects were instructed (1) not to exercise, (2) not to take a shower, and (3) to relax and straighten out the arm during each recording interval for the entire 24 h period.

Individual ambulatory blood pressure measurements were reviewed for missing and erroneous readings. Readings were purged if (1) data was missing, (2) systolic blood pressure was lower than diastolic blood pressure or if systolic blood pressure was >240 or <50 mmHg, (3) if diastolic blood pressure was >140 or <40 mmHg, or (4) if heart rate was >150 or <40 beats per minute. System tagged data were purged if (1) systolic blood pressure deviated $\pm 50$ mmHg, (2) diastolic blood pressure deviate $\pm 20$ mmHg, or (3) heart rates deviated $\pm 30$ beats from the surrounding values.[22] Systolic and diastolic blood pressure were averaged for 24 h, daytime (0600–2200 h), and nighttime (2200–0600 h).

The area of blood pressure reduction was calculated to determine the duration of blood pressure reduction. The area of blood pressure reduction was defined as the area between the control and exercise blood pressure curves.[23] The area between the blood pressure curve and the time axis ($x$-axis) was calculated by summing the area of successive trapezoids, corresponding to each blood pressure reading. The total area below the treatment curve was subtracted from the total area under the control curve to obtain the area between the curves.

### Statistical methods

Values were expressed as means $\pm$ standard errors of the means (s.e.m.). The level of significance was set at $P<0.05$. Independent $t$-tests were performed to compare the demographics of subjects between non-dipping and dipping hypertensive groups. The demographic variables were sex, age, body mass index, screening systolic and diastolic blood pressure and $VO_{2peak}$. A two-way ANOVA (Dipping Status × Time of Exercise) with repeated measures was performed using the blood pressure reduction as dependent ambulatory blood pressure variables: difference between control and exercise systolic and diastolic blood pressure (mmHg) for daytime, nighttime and 24 h. Paired $t$-tests were used to compare the first and last 12 h period of the area of the blood pressure reduction for Dippers and Non-Dippers. All statistical analyses were performed using SPSS software (SPSS 11.0).

## Results

### Subjects

In all, 19 hypertensive adults were screened; five were found to be ineligible during the screening process. A total of 14 hypertensive adults who were qualified based on screening blood pressures, ambulatory blood pressures, exercise testing, and nocturnal patterns participated in the study. Subjects were classified as Dippers ($n=9$) or Non-Dippers ($n=5$) based on the control ambulatory blood pressure monitoring sessions. All of Dippers and Non-Dippers exhibited the nocturnal requirements for their respective groups.

Demographics of the subjects are summarized in Table 1. None of the demographic variables were different between Dippers and Non-Dippers except for average 24 h and nighttime blood pressure. Both of these variables were higher in the Non-Dippers

**Table 1** Demographics of subjects

| | *Dippers (n = 9)* | *Non-dippers (n = 5)* | *t-values/P-values* |
|---|---|---|---|
| Sex (men/women) | 6/3 | 2/3 | |
| Race | 8 Caucasian<br>1 Asian | 3 Caucasian<br>1 Asian<br>1 Native American | |
| Age (years) | 55.6 ± 1.47 | 58.2 ± 3.32 | −0.85<br>0.41 |
| Weight (kg) | 80.3 ± 6.09 | 78.5 ± 7.13 | 0.19<br>0.86 |
| Height (cm) | 172.6 ± 2.30 | 166.4 ± 5.49 | 1.24<br>0.24 |
| Body mass index ($kg/m^2$) | 26.7 ± 1.47 | 28.2 ± 1.87 | −0.63<br>0.54 |
| $VO_{2peak}$ ($ml/kg^{-1}/min^{-1}$) | 29.6 ± 1.28 | 25.0 ± 2.37 | 1.91<br>0.08 |
| Activity level (active/sedentary) | 7/2 | 4/1 | 0.09<br>0.93 |
| Screening systolic/diastolic blood pressure (mmHg) | 144.4 ± 3.50/<br>88.0 ± 2.08 | 141.6 ± 4.17/<br>91.2 ± 1.20 | 0.50/−1.08<br>0.62/0.30 |
| 24-h systolic/diastolic blood pressure (mmHg) | 143.1 ± 2.41*/<br>83.4 ± 1.01 | 150.4 ± 1.29/<br>83.5 ± 1.71 | −2.16/−0.30<br>0.04/0.98 |
| Daytime systolic /diastolic blood pressure (mmHg) | 147.5 ± 2.53/<br>86.1 ± 1.23 | 151.3 ± 1.29/<br>85.4 ± 1.71 | −1.07/0.31<br>0.30/ 0.76 |
| Nighttime systolic/diastolic blood pressure (mmHg) | 123.4 ± 2.18*/<br>73.1 ± 1.47 | 146.3 ± 2.68/<br>76.7 ± 2.50 | −6.47/−1.34<br>0.001/0.19 |

Values were expressed as means ± s.e.m.
*Denotes significant differences at $P < 0.05$.

because of the elevated nocturnal blood pressure. Two of subjects were taking combinations of antihypertensive medications (angiotensin converting enzyme inhibitor, calcium channel blocker, and beta blocker), and six of subjects were taking a single antihypertensive medication (angiotensin converting enzyme inhibitor, calcium channel blocker and beta blocker).

As part of the screening process, all of the subjects performed a maximal exercise test. One of the subjects who did not meet the screening criteria was disqualified with the exercise test by exercise-induced headache. The 14 subjects who were qualified for the study performed a maximal voluntary effort on the exercise test as verified by reaching 103.4 ± 2.09% predicted maximal heart rate.

### Exercise stimulus

Each exercise session was separated by 9.8 ± 0.26 days. Exercise intensities were similar between morning (52.0 ± 0.21% of $VO_{2peak}$) and evening exercise (54.3 ± 0.26% of $VO_{2peak}$). Both Dippers and Non-Dippers also exhibited similar exercise intensities for both morning (52.4 ± 0.87%; 51.5 ± 1.88% of $VO_{2peak}$) and evening (53.7 ± 0.93%; 54.8 ± 2.55% of $VO_{2peak}$) exercise, respectively.

### Ambulatory blood pressure

Table 2 summarizes the ambulatory blood pressure monitoring sessions for each group and each treatment. The duration of the ambulatory blood pressure monitoring sessions averaged 24.1 ± 0.9 h for both groups for all the treatment conditions. An average of 101.0 ± 12.2 blood pressures were taken for each ambulatory monitoring session; 85.8 ± 8.7% of the pressures were used in the analysis. Dippers and Non-Dippers did not differ in the number of pressures taken and the percent analysed for each of the four monitoring sessions. Even though the average duration of sleep was 6.5 ± 1.1 h for both groups for all four treatment conditions, the time to go to bed ranged from 2100 to 0200 and the time to wake-up ranged from 0320 to 0900. These times and duration of sleep did not differ among the treatments or between the groups.

**Table 2** Ambulatory monitoring

| *Group* | *Morning control* | *Morning exercise* | *Evening control* | *Evening exercise* |
|---|---|---|---|---|
| *Duration of monitoring session (h)* | | | | |
| Dippers | 24.3 ± 1.19 | 24.6 ± 1.33 | 24.1 ± 0.64 | 24.1 ± 0.6 |
| Non-Dippers | 23.8 ± 0.24 | 23.7 ± 0.43 | 23.7 ± 0.23 | 23.9 ± 0.2 |
| *Number of blood pressure measurements* | | | | |
| Dippers | 102.4 ± 14.65 | 104.3 ± 12.34 | 98.8 ± 8.66 | 101.4 ± 6.8 |
| Non-Dippers | 100.2 ± 5.17 | 96.2 ± 6.30 | 96.4 ± 5.03 | 108.8 ± 32.1 |
| *Percent of blood pressure measurements analysed* | | | | |
| Dippers | 80.3 ± 12.82 | 85.7 ± 6.83 | 88.5 ± 8.47 | 84.7 ± 5.6 |
| Non-Dippers | 85.9 ± 9.08 | 87.2 ± 10.5 | 85.8 ± 4.59 | 92.3 ± 3.0 |

Values were expressed as mean ± s.e.m.

The hourly reductions in blood pressure associated with morning and evening exercise are illustrated in Figure 1 for dipping (Panel A) and nondipping hypertension (Panel B) for the 24 h clock. A two-way ANOVA (dipping status × time of exercise) with repeated measures using the blood pressure reduction reveals that a significant two-way interaction between dipping status and time of exercise was found for the reduction in nighttime systolic blood pressure (see Table 3). Simple effects found that Non-Dippers exhibited a significantly greater reduction in average nighttime systolic blood pressure than Dippers following both morning ($F=13.43$; $P=0.001$) and evening exercise ($F=7.13$; $P=0.013$). No significant two-way interaction was found in either 24 h or daytime systolic blood pressure reductions (Table 3) as well as for any diastolic blood pressure reductions.

The data presented in Table 4 address the first two hypotheses. In Table 4 daytime and nighttime systolic blood pressure reductions following morning and evening exercise were compared between dipping and nondipping hypertension. Non-Dippers exhibited a significantly greater reduction in average nighttime systolic blood pressure than Dippers following evening exercise ($F=7.13$; $P=0.013$). No statistical difference was found between dipping status and time of exercise for average daytime blood pressure reductions following exercise ($F=0.001$; $P=0.991$).

The data presented in Table 5 address the last two hypotheses. Table 5 illustrates the reduction in average 24 h blood pressure for Dippers and Non-Dippers following morning and evening exercise. The reduction in 24 h systolic blood pressure was not affected by interaction between the time exercise and dipping status ($F=0.08$; $P=0.778$).

Figure 2 illustrates the areas for the 24 h blood pressure reduction starting from the end of exercise. For the Non-Dippers, both 12 h periods contributed to the average 24 h reduction in blood pressure because the area of the reduction from the first 12 h period following morning ($t=-0.41$; $P=0.700$) and evening ($t=0.61$; $P=0.583$) exercise was similar to

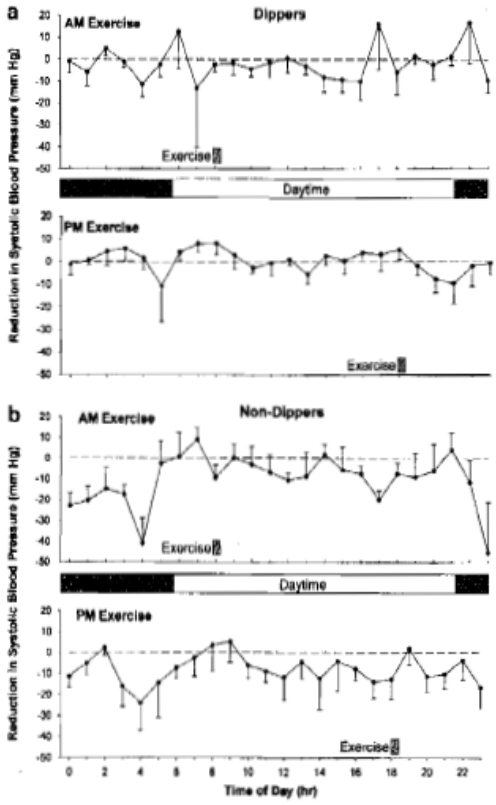


**Figure 1** Hourly blood pressure reduction associated with morning (AM) and evening (PM) exercise in dipping (a) and nondipping (b) hypertension for the 24 h clock. Values are expressed as mean ± s.e.m. Exercise periods are illustrated by shaded areas. Nighttime and daytime periods are also illustrated based on TOD. The data points following the shaded exercise included only those blood pressures that followed the exercise treatment.

**Table 4** Daytime and nighttime reduction in systolic blood pressure following morning and evening exercise in dipping and nondipping hypertension

| | *Dippers* | *Non-Dippers* |
|---|---|---|
| Nighttime average following evening exercise (mmHg) | −0.30 ± 1.7* | −11.50 ± 3.85 |
| Daytime average following morning exercise (mmHg) | −5.67 ± 2.59 | −6.00 ± 1.23 |

Values were expressed as means ± s.e.m.
*Denotes significant group differences at $P<0.05$.

**Table 3** A two-way ANOVA (dipping status × time of exercise) with repeated measures using the blood pressure reduction

| | *Daytime SBP* | | *Nighttime SBP* | | *24 h SBP* | |
|---|---|---|---|---|---|---|
| Dipping status | $F=0.07$ | $P=0.790$ | $F=3.19$ | $P=0.100$ | $F=0.38$ | $P=0.547$ |
| Time of exercise | $F=0.65$ | $P=0.434$ | $F=9.22$ | $P=0.010$ | $F=1.85$ | $P=0.199$ |
| Dipping status × time of exercise | $F=0.001$ | $P=0.991$ | $F=4.84$* | $P=0.048$ | $F=0.08$ | $P=0.778$ |

SBP: systolic blood pressure.
*Denotes significant group differences at $P<0.05$.

**Table 5** The 24 h reduction in systolic blood pressure following morning and evening exercise in dipping and nondipping hypertension

| | *Morning exercise (mmHg)* | *Evening exercise (mmHg)* |
|---|---|---|
| Dippers | −5.56 ± 2.27 | 0.11 ± 2.29 |
| Non-Dippers | −7.22 ± 2.10 | −7.00 ± 3.16 |

Values were expressed as means ± s.e.m.

the last 12 h period. Similar findings were exhibited for the Dippers who exercised in the morning ($t = -3.56$; $P = 0.730$). For the Dippers who exercised in the evening, however, the contribution of the two 12 h periods is not as clear. The second 12 h period actually exhibited a higher systolic blood pressure following exercise although it is not statistically higher ($t = 0.68$; $P = 0.583$).

## Discussion

The purpose of this study was to observe the effects of TOD for exercise on the reduction of ambulatory blood pressure in dipping and nondipping hypertension. We found that (1) evening exercise exhibited a greater reduction in nighttime systolic blood pressure for Non-Dippers than for Dippers, (2) morning exercise exhibited similar daytime systolic blood pressure reductions for Dippers and Non-Dippers, and (3) morning and evening exercise treatments exhibited similar 24 h systolic blood pressure reduction for both dipping and nondipping hypertension. The additional important findings in this study include: (1) Non-Dippers respond to exercise treatment, (ie both morning and evening exercise produced a reduction in nighttime systolic blood pressure in Non-Dippers) and (2) the duration of the blood pressure reduction appears to be greater than 12 h. Table 6 summarizes these findings in relationship to the literature.

Non-Dippers were investigated in the study because (1) they have been identified as nonresponders to exercise[12] and (2) non-dipping hypertension is associated with more serious end-organ damage and higher incidence of cardiovascular complications than Dippers.[11] A single bout of exercise was chosen for this study because it may be the initial step to investigate the effectiveness of exercise on blood pressure reduction in populations previously identified as nonresponders.[24] Training studies may not be justified without demonstrating an acute response first. Furthermore, the utilization of acute exercise responses allows for more efficacious study into possible variations in the exercise prescription for nonresponders. One of the possible variations in the exercise prescription for the nondipping hypertensive patients was considered to be the TOD for exercise.

### Subjects

The subjects in this investigation were similar to subjects found in exercise and blood pressure reduction studies.[8] The nocturnal dipping status in hypertension was confirmed by the two control ambulatory blood pressure monitoring sessions. The reproducibility of the dipping and nondipping hypertension is consistent with the study by Nami and collegues.[12] Systolic blood pressure reductions were found in average 24 h, daytime and nighttime systolic blood pressure. No significant reduction was found for diastolic blood pressure. The blood pressure reductions of the subjects are consistent with other studies utilizing a single bout of exercise.[15,25] The number of subjects were adequate for all of significant findings with $>0.94$ of power and $>0.32$ of effect size ($\omega^2$). Null findings of this study could be due in part to the number of subjects and, as such, a high likelihood of Type II error could exist.

### Ambulatory blood pressure monitoring

Control ambulatory blood pressure monitoring was performed twice, once in the morning and once in the evening corresponding to the two exercise sessions. In our laboratory, we have found the TOD to begin ambulatory blood pressure monitoring affects blood pressure outcomes.[26] The control monitoring sessions starting the morning have been found to have higher average blood pressures and blood pressure than monitoring sessions starting in the evening. A similar trend was seen in these data, however, no significant difference in the three average blood pressure variables was found between the two control sessions in this study.

There are several important findings from this study. Not only were Non-Dippers found to respond to exercise treatment, but also Non-Dippers reduced their nighttime systolic blood pressure (−10.1 ± 2.70 mmHg) despite the TOD for exercise. The reduction in systolic blood pressure in Non-Dippers contradicts the findings of Nami and collegues,[12] who reported aerobic exercise training failed to reduce blood pressure in nondipping hypertension.

In the study,[12] Nami and colleagues investigated salt intake and other metabolic variables and found no relationship among the inability to reduce blood pressure with exercise and the other confounding variables. They reported good subject adherence to their study protocol. Our studies differed in the subject demography, exercise treatment, and use of a control group. Our subjects had higher blood pressures, were older, and some had been treated with antihypertensive medications. It would seem obvious that our subject would exhibit a greater reduction in blood pressure because higher blood pressures exhibit greater reductions.[9] On the other hand, Nami and colleagues found a blood

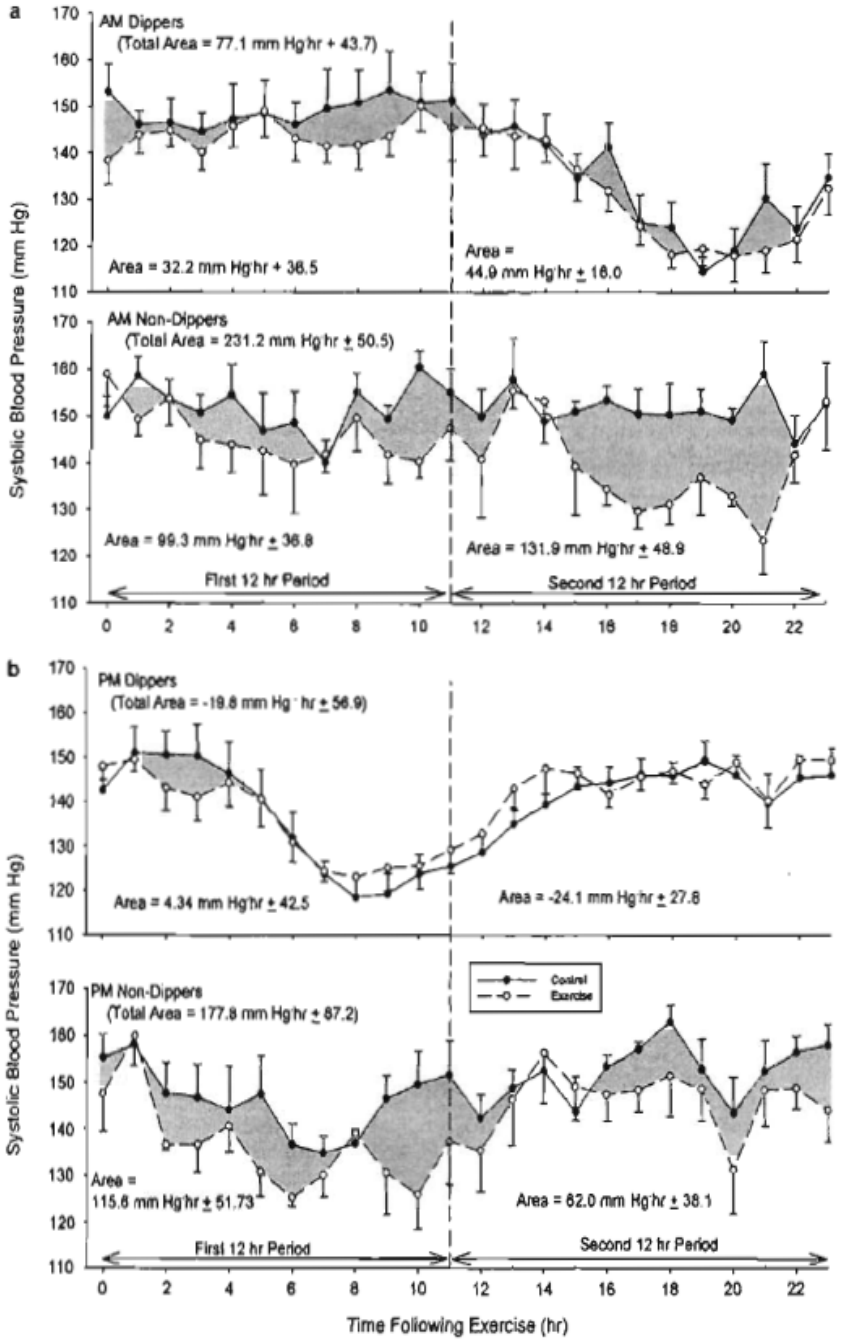


Figure 2 Area of blood pressure reduction (shaded) following morning (AM; a) and evening (PM; b) exercise in dipping and nondipping hypertension. Values are expressed as mean ± s.e.m.

pressure reduction in their Dippers (24 h, daytime and nighttime systolic blood pressures: 130.6 ± 1.8, 135.9 ± 0.8, and 120.0 ± 0.8 mmHg) who also had lower pressures than our Dipping subjects. Our subjects were approximately 25 years older than Nami's (Dippers = 29.5 ± 1.16 years; Non-Dippers = 31.4 ± 1.9 years). Middle-aged hypertensive subjects have a tendency to decrease blood pressure somewhat

**Table 6** A summary of current literature and contributions of this study

*What is known on this topic*

1. Endurance exercise training lowers blood pressures in hypertensive patients[8-10]
2. Nocturnal nondipping hypertensive patients (Non-Dippers: defined as <10% reduction in average nighttime blood pressure compared to average daytime blood pressure)[11] have been identified among the nonresponders to exercise training[12]
3. A more effective exercise programme for Non-Dippers may be warranted
4. The reduction in blood pressure following a single bout of exercise has been reported to persist for up to 11–12 h under free-living conditions for systolic blood pressure (5–8 mmHg) and/or up to 4–8 h for diastolic blood pressure (6–8 mmHg)[13-17]
5. Exercise treatment prior to the period of highest blood pressure elevation may result in a more attenuated response because greater blood pressure reductions can be found in higher pressures[18]

*What this study adds*

1. This study observed the effects of the TOD for exercise on the reduction of ambulatory blood pressure in dipping and nondipping hypertension
   (a) Evening exercise exhibited a greater reduction in nighttime systolic blood pressure for Non-Dippers than for Dippers
   (b) Morning exercise exhibited similar daytime systolic blood pressure reductions for Dippers and Non-Dippers
   (c) Morning and evening exercise treatments exhibited similar 24 h systolic blood pressure reduction for both dipping and nondipping hypertension
2. The additional important findings in this study include:
   (a) Non-Dippers respond to exercise treatments. Nighttime systolic blood pressure for Non-Dippers was reduced despite of time of day for exercise — that is either morning or evening exercise
   (b) The duration of the blood pressure reduction appears to be greater than 12 h

more and somewhat more consistently than younger hypertensive subjects.[8]

Different exercise stimuli can produce different blood pressure responses.[9] The mode (cardiovascular), duration (60 min) and intensity (40–60%) of Nami's stimulus[12] were not only similar to ours, but within the guidelines for appropriate exercise treatment.[4] Our exercise treatment differed from Nami's in that ours was acute and Nami's was training. Yet, our results cannot be attributed to these differences because in blood pressure, the acute response reflects the training response.[24] On the other hand, Nami and colleagues did not include the control group in their study, which made it hard to interpret the effects of exercise training on blood pressure. Our subjects served as their own controls.

Another significant finding in our study was the nature of the blood pressure reduction in Dippers and Non-Dippers. Not only did the Non-Dippers exhibit a greater nighttime reduction in systolic blood pressure than the Dippers following evening exercise, but the Non-Dippers exhibited similar daytime systolic blood pressure reduction as the Dippers despite morning or evening exercise, as illustrated in Tables 3 and 4. Dippers were not expected to reduce average nighttime blood pressure following evening exercise in the same magnitude as the Non-Dippers because the average nighttime blood pressure for the Dippers was near normal ($124.4 \pm 3.30$ mmHg). It is well documented that higher blood pressures exhibit greater reductions following exercise.[17,27] In this study, a significant correlation ($r = 0.58$; $P = 0.002$) was also found between baseline blood pressure and daytime and nighttime blood pressure reduction following exercise. Furthermore, the average nighttime blood pressure reduction was greater in the Non-Dippers who presented with higher pressures ($143.5 \pm 1.68$–$132.0 \pm 2.60$ mmHg) than in the Dippers who presented with near normal nighttime blood pressures ($124.4 \pm 3.12$–$124.1 \pm 1.68$ mmHg).

The nighttime reduction in blood pressure for Non-Dippers who exercised in the morning was not expected because the primary reduction in blood pressure following exercise had been reported to be 12 h.[13-17] It appears, however, as though the reduction in blood pressures found in this study exceeded this 12 h period, similar to the findings of Brandao-Randon and colleagues[4,25] who reported the 22 h postexercise blood pressure reduction in elderly hypertensive patients. Most investigators may not have detected a reduction in blood pressure beyond the first 12 h because of the criteria used to estimate the duration of postexercise hypotension. In these studies, the duration of the blood pressure reduction was determined to be the time where the hourly blood pressures were no longer significantly different (control *vs* exercise, or pre-*vs* exercise). Whereas, Brandao-Randon *et al*[4,25] reported significant differences for average pressures for specific periods of the day (ie daytime and nighttime) which accounted for the entire 22 h. We found similar reductions for average 24 h ($-5.3 \pm 1.12$ mmHg; $F = 9.78$; $P = 0.009$), daytime ($-4.4 \pm 1.02$ mmHg; $F = 7.81$; $P = 0.016$), and nighttime ($-5.9 \pm 1.62$ mmHg; $F = 10.72$; $P = 0.004$). It is possible for total 24 h average blood pressures to be significantly lower because of the magnitude of the first 12 h period of reduction even though the second 12 h period is not significantly different.

To investigate this effect further, we compared the first 12 h period and the last 12 h period blood pressure reduction by comparing the area between the control and exercise blood pressure curves (Figure 2). The 24 h reduction in systolic blood pressure following exercise appears to be a true phenomenon and not influenced by

the magnitude of the reduction during the first 12 h period. The extension of the reduction beyond the first 12 h period may explain why the reductions in 24 h systolic blood pressure were not affected by the TOD for exercise in both Dippers and Non-Dippers.

In conclusion, Non-Dippers responded to exercise treatment. Dippers and Non-Dippers, however, responded differently to exercise treatments presented at different times of day. Non-Dippers decreased nighttime systolic blood pressure following exercise whereas Dippers did not. Finally, the reduction in systolic blood pressure found in this study persisted up to 24 h after exercise in Non-Dippers who exercised in the morning or the evening and in Dippers who exercised in the morning.

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***APPENDIX H - DISSERTATION PROPOSAL***

***PROBLEM***

High blood pressure, or hypertension, is a major risk factor for many cardiovascular diseases including stroke (35), coronary artery disease (35), congestive heart failure (64), and end-stage renal disease (26). The prevalence of hypertension increases with advancing age. According to the Framingham Heart Study (63), 90% of individuals with normal blood pressure at 55 to 65 years of age will develop hypertension, defined as blood pressure of 140/90 mm Hg or greater or use of antihypertensive medications, over the course of their lifetime. The mortality from both ischemic heart disease and stroke increases two-fold for each 20 mm Hg increase in systolic or 10 mm Hg increase in diastolic blood pressure above 115 mm Hg of systolic and 75 mm Hg of diastolic blood pressure (29). In addition, there is a two-fold increase in relative risk from cardiovascular disease with systolic blood pressure of 130 to 139 mm Hg and with diastolic blood pressure of 85 to 89 mm Hg compared with a blood pressure of below 120/80 mm Hg (63).

In 2003 the new classification of blood pressure, prehypertension, was introduced by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 1) to identify individuals who are at high risk of developing hypertension, 2) to decrease the rate of progression of hypertension or 3) to prevent hypertension and its related cardiovascular disease for those individuals (7). Prehypertension is defined as systolic blood of 120 to 139 mm Hg and/or diastolic blood pressure of 80 to 89 mm Hg. Approximately 45 million Americans have prehypertension (6). Early intervention by adopting

healthy lifestyles has been proposed for individuals with prehypertension to lower blood pressure and to delay or to prevent hypertension entirely. The new exercise prescription, the accumulation of moderate physical activity on most if not all days of the week, has been advocated as a lifestyle modification for the prevention of hypertension (3, 7) by several health organizations, including the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (6), the American Heart Association (16), and the American College of Sports Medicine (2). There are limited studies, however, supporting the daily accumulation of physical activity as a means to treat prehypertnesion and to prevent progression to hypertension. This recommendation has been formulated based on the epidemiological evidence (5, 42) and a few clinical studies (10, 38) compared to the literature supporting traditional exercise recommendation (20 to 60 minutes of moderate aerobic exercise at 40 to 70% of maximal oxygen consumption, $VO_2$max) (4, 12, 13, 18, 31, 66, 67, 69). Thus, studies are warranted to investigate the effectiveness of the daily accumulation of physical activity on the treatment for prehypertension and the prevention of hypertension.

There are only a few studies to investigate the effects of physical activity on blood pressure reduction in prehypertension. Dunn et al. (10) compared the 24-month intervention effects of a lifestyle physical activity (accumulation of 30-minutes of any type of activity) with traditional structured exercise (50-85% of $VO_2$peak at 20-60 minutes) on cardiorespiratory fitness and cardiovascular disease risk factors. They reported significant reductions in systolic (3.63 mm Hg

and 3.26 mm Hg) and diastolic (5.38 mm Hg and 5.14 mm Hg) blood pressure with physical activity and structured exercise, respectively. Moreau et al. (38) also found a reduction in systolic blood pressure following 12 weeks (6 mm Hg) and 24 weeks (additional 5 mm Hg) of a walking program (3 km/day) in 24 post-menopausal women with prehypertension and stage 1 hypertension. In both studies it was unclear the physical activities were performed all at once and they were accumulated throughout the day. Furthermore, the duration and magnitude of blood pressure reduction were not investigated. Thus, the effect of accumulated several short bouts compared to one long continuous bout of physical activity on blood pressure reduction could not be determined from these studies.

The effects of the accumulation of physical activity on health outcomes have been investigated with fractionated exercise (1, 9, 17, 24, 40). Fractionation of exercise is the term used to investigate different patterns (one continuous long versus several short bouts of exercise) and/or intensity of exercise (moderate/hard versus low intensity of exercise) (20). Long versus several short bouts of exercise has been studied on variables of health and fitness, such as $VO_2$max (1, 24), blood lipids (17, 40), glucose/insulin dynamics (17), bone mass (51), and exercise adherence (53). While it appears that several short bouts of exercise improves functional capacity ($VO_2$max) (20), and blood lipids (17, 40), there is little information on the effects of fractionated exercise on blood pressure.

There are only one study to date has demonstrated the effects of one long versus several short bouts or fractionated exercise on blood pressure by Murphy and Hardman (39) as a secondary outcome. They investigated training effects of short and long bouts of brisk walking in sedentary women. Women were randomly assigned to three 10-minute walks (n=12), one 30-minute walk (n=12) at 70 to 80 % of maximal heart rate for 10 weeks or control group (no walk, n=10). The short bouts of exercise group reduced systolic blood pressure by 7.4+7.3 mm Hg and the long bout exercise group reduced systolic blood pressure by 4.6+5.9 mm Hg. Yet, the blood pressure reduction was not statistically significant. It might be possibly due to lack of statistical power in the study (n=12). Thus, more investigation is warranted to explore the effects of one long versus the accumulation of several short bouts of exercise on blood pressure reduction as a primary outcome.

A sustained reduction in resting blood pressure following a single bout of aerobic exercise has been defined as post exercise hypotension (25). Post exercise hypotension resulted from traditional exercise prescription is sustained for a prolonged period of time under free-living conditions up to 11 to 12 hours for systolic blood pressures (5-8 mm Hg) and/or up to 6 to 8 hours for diastolic blood pressure (6-8 mm Hg) (25, 34, 47, 65, 67) in hypertensive individuals. The duration and magnitude of post exercise hypotension resulting from the accumulation of physical activity are unknown.

The mechanisms of post exercise hypotension are not fully understood at this time, however, sympathetic modulation has recently received more focus as

one of the possible mechanisms of post exercise hypotension (19, 31). Sympathetic modulation describes changes in the balance between sympathetic and parasympathetic influences (50). Power spectral analysis of the RR interval of the electrocardiogram has emerged as a method to measure sympathetic modulation in hypertension (43, 45, 50, 57). A decreased sympathetic activity and/or an increased parasympathetic activity would be considered as an improvement of sympathetic modulation. Exercise training has been found to improve sympathetic modulation measured by power spectral analysis of heart rate variability in various populations (21-23, 36, 37, 54, 55, 61, 62) including hypertensive individuals (44, 58). Sympathetic modulation measured by power spectral analysis of heart rate variability has not been studies extensively during post exercise hypotension (27, 33). MacDonald et al. showed increased parasympathetic activity after acute exercise (70% of $VO_2$peak for 30 minutes) using short-term heart rate variability (33) while Legramante et al. failed to see the changes in sympathetic modulation after maximal exercise test (27). Studies using long-term heart rate variability, however, would be of interest in post exercise hypotension studies because post exercise hypotension persists up to 11 to 12 hours under free-living conditions (25, 34, 47, 65, 67). Furthermore, a single bout of submaximal exercise improved sympathetic modulation measured by heart rate variability at hour six after cessation of exercise in healthy subjects (49). No study has been attempted to explore the autonomic mechanisms of post exercise hypotension during free-living conditions.

## *PURPOSE OF THE STUDY*

The purpose of this study is (1) to compare the blood pressure reduction following the accumulation of short bouts of exercise and one long bout of exercise in adults with prehypertension, and (2) to compare the blood pressure reduction following each successive short bout of exercise in adults with prehypertension. In addition, sympathetic modulation will be investigated as a possible mechanism for the blood pressure reduction following exercise in adults with prehypertension.

## *HYPOTHESES*

### The Accumulation of Short Bouts versus One Long Bout of Exercise

1. The blood pressure reduction following the accumulation of four short bouts of exercise will not be different from the reduction following one long bout of exercise in adults with prehypertension.
    a. The duration of blood pressure reduction from control following the accumulation of four short bouts of exercise will not be different from the duration of the reduction from control following one long bout of exercise in adults with prehypertension.
    b. The magnitude of blood pressure reduction from control following the accumulation of four short bouts of exercise will not be different from the magnitude of the reduction from control following one long bout of exercise in adults with prehypertension.

2. The sympathetic modulation, measured by power spectral analysis of the RR interval of the electrocardiogram, will be associated with the blood pressure reduction following the accumulation of short bouts of exercise and one long bout of exercise in adults with prehypertension.
    a. The magnitude of blood pressure reduction will be negatively associated with the change in low frequency component of the power spectral analysis of the RR interval in adults with prehypertension.
    b. The magnitude of blood pressure reduction will be positively associated with the change in high frequency component of the power spectral analysis of the RR interval in adults with prehypertension.
    c. The magnitude of blood pressure reduction will be negatively associated with the change in low to high frequency ratio of the power spectral analysis of the RR interval in adults with prehypertension.
3. The association between blood pressure reduction and sympathetic modulation following the accumulation of four short bouts of exercise will not be different from the association following one long bout of exercise in adults with prehypertension.
    a. The association between the magnitude of blood pressure reduction and the change in sympathetic modulation (measured by low and high frequency component as well as the low to high

frequency ratio of the power spectral analysis of the RR interval) following the accumulation of four short bouts of exercise will not be different from the association between the magnitude of blood pressure reduction and the change in sympathetic modulation following one single long bout of exercise.

**Successive Short Bouts of Exercise**

1. The magnitude of blood pressure reduction following each successive short bout of exercise will be different in adults with prehypertension.
    a. The magnitude of blood pressure reduction from baseline following each successive short bout of exercise will be greater for each successive short bout of exercise in adults with prehypertension.
2. The sympathetic modulation, measured by power spectral analysis of the RR interval of the electrocardiogram, will be different following each successive short bout of exercise in adults with prehypertension.
    a. The low frequency component of the power spectral analysis of the RR interval following each short bout of exercise will be lower each successive short bout of exercise in adults with prehypertension.
    b. The high frequency component of the power spectral analysis of the RR interval following each short bout of exercise will be higher each successive short bout of exercise in adults with prehypertension.

c. The low to high frequency ratio of the power spectral analysis of the RR interval following each short bout of exercise will be lower each successive short bout of exercise in adults with prehypertension.

***STUDY DESIGN***

The study will be a within-subjects design. Each prehypertensive subject will receive all of the treatment conditions in a randomized order. The treatment conditions will be composed of (a) the accumulation of four short bouts of exercise treatment (four 10-minute treadmill walk at 50% of $VO_2$peak at least 50-minute apart), (b) one long bout of exercise treatment (40-minute treadmill walk at 50% of $VO_2$peak), and (c) a control treatment. The two exercise treatments will be separated by at least seven days to avoid a training effect. Following each treatment blood pressure will be measured for 12 hours during activities of daily living using ambulatory blood pressure monitoring. Changes in sympathetic modulation, measured by power spectral analysis of the RR interval of the electrocardiogram, will be investigated as a possible mechanism of blood pressure reduction following exercise treatments. The amount of physical activities in each treatment will be assessed using an accelerometer to statistically control physical activity as a confounding factor for the blood pressure reduction seen in the study.

Although the timing of the exercise treatments in this study may not appear to be applicable to daily living, this study design is based on diurnal variations in blood pressure and the nature of blood pressure reduction through

exercise treatments. Greater blood pressure reductions can be found for higher blood pressures (18). Blood pressure is highest in the afternoon/evening hours and lowest in the nighttime (7). This design, by completing the treatments by 1:00 p.m., optimizes the ability to detect blood pressure changes, i.e. the afternoon/evening elevations, which is the highest point of the diurnal rhythm. The chances of detecting blood pressure reductions may be compromised by the low, near normal nocturnal pressures (28, 46, 68) if the stimulus would end in the evening. Therefore, both treatments will end prior to this time, allowing for the most optimal approach to find a treatment effect.

***SUBJECTS***

At least 20 adults with prehypertension will be recruited for this study. The number of subjects has been estimated based on power analysis (46) performed on previous study for blood pressure with a similar study design (41) using physical activity treatment in perhypertensive adults (power:>0.80; effect size using partial eta squared:>0.41). Inclusion criteria for adults with prehypertension will be a mean systolic screening blood pressure 120 to 139 mmHg and/or a mean diastolic blood pressure 80 to 89 mmHg taken from at least two readings on two separate days, three days apart. Subject exclusion criteria will include: 1) significant cardiovascular disease; 2) significant dysrhythmia (66, 67); 3) brachial artery bruits (66, 67); 4) cardiac or renal transplant patients (66, 67); or 5) medications such as anti-arrhythmic drugs or

low dose muscarinic receptor blockers including atropine and scopolamine that affect the heart rate variability (57).

Clearance by the subjects' primary physician will be required prior to participation in the study. The study is approved by the Bloomington Campus Committee for the Protection of Human Subjects at Indiana University. Each subject will be given informed consent prior to participation in the study. The study will be carried out in the Clinical Exercise Physiology Laboratory in the Department of Kinesiology at Indiana University.

***PROCEDURE***

Procedures include: (1) blood pressure screening; (2) maximal graded exercise test; and (3) measurements of ambulatory blood pressure, ambulatory electrocardiogram (EKG) and accelerometer: (a) following the accumulation of four short bouts of exercise treatment (four 10-minute treadmill walks at 50% $VO_2$peak, at least 50-minute apart), (b) following one long bout of exercise treatment (40-minute treadmill walk at 50% $VO_2$peak), (c) following each separate short bout of exercise for 50 minutes in a seated position, and (d) following corresponding time of the non-exercise control treatment. Ambulatory blood pressure and ambulatory EKG monitors will be taken off during the exercise sessions and will be restarted after the exercise treatments. An accelerometer will be worn during the exercise treatments. The order of all three treatments will be randomized. The two exercise days will be separated by at least seven days (48).

## *METHODOLOGY*

### Blood Pressure Screening

For all subjects three blood pressures will be taken in the seated position on two separate days, three days apart (a total of six measurements) using a mercury sphygmomanometer. Subjects will be seated for at least five minutes in a chair, with feet on the floor, and arm supported at heart level (7). Subjects will be asked to avoid caffeine, exercise and smoking for at least 30 minutes prior to measurement (7). An appropriate sized cuff (cuff bladder encircling at least 80% of the arm) will be used to ensure accuracy (7). On the first day blood pressure will be taken in both arms to detect possible differences due to peripheral vascular disease (70, 71). The arm with highest blood pressure will be used for the screening (70).

### Maximal Graded Exercise Test

The purpose of maximal graded exercise test is to measure physical work capacity to ensure the exercise intensity for the treatments. A fasting blood draw and a standard resting 12 lead electrocardiogram (EKG) will precede the maximal graded exercise test to establish risk for exercise (2). Body weight (kg) and height (cm) will be determined to the nearest value of 0.1. The graded exercise test will be performed on a treadmill with a speed between 2.5 and 4.0 mph at 0% grade. The speed will remain constant throughout the test while the grade increase 2.0% every minute until a maximal voluntary effort is achieved. Blood pressure (by auscultation) and heart rate (by EKG) will be measured every

minute. The EKG will be monitored continuously. Expired gases will be measured on-line breath-by-breath using a Sensor Medics 2900 Metabolic Cart. Peak oxygen uptake ($VO_2$peak) will be obtained during the symptom-limited maximal exercise test. $VO_2$peak is defined as the highest $VO_2$ obtained from the symptom-limited maximal exercise test.

**Treatments**

The treatments include 1) one long continuous bout of exercise; 2) four short bouts of exercise; and 3) one control. The mode of exercise will be walking on a motorized treadmill and the intensity of each exercise bout will be at 50% $VO_2$peak. Oxygen uptake ($VO_2$) will be measured during the 4th through the 6th minutes of each walk to confirm the intensity of exercise. The work rate will be adjusted if it is not within $\pm$10% of the target $VO_2$. Then, $VO_2$ will be measured during the 6th through the 8th minutes of the next work interval to confirm the new exercise intensity. Heart rate (via EKG) and blood pressure (via auscultation) will be measured throughout the exercise treatments.

One Long Bout of Exercise Treatment: The duration of the one long bout of exercise will be 40-minutes. The one long bout of exercise will begin between 1200 and 1300 hrs.

Four Short Bouts of Exercise Treatment: The duration of each short bout of exercise stimulus will be 10-minute; the first between 0900 and 0930 hours, the second between 1000 and 1030 hours, the third between 1100 and 1130 hours, and the last between 1200 and 1230 hours to end the time as one long bout.

Control Treatment: For the control treatment the subject will report to the lab between 1200 and 1300 hours approximately 15 minutes before the time when the monitors would be activated for the exercise treatments. Control data will be collected for the same time period as the other two treatments. No sham rest period will be used for the control treatment to simulate the time of attention given to the subject during exercise treatments because rest if considered an intervention itself.

**24-hour Ambulatory Blood Pressure Monitoring**

The Accutracker II (Suntech Medical Instruments, Inc., Raleigh, NC) will be used for all ambulatory measurements. The Accutracker II has been validated in accordance to the standards of the British Hypertension Society and the American Association for Medical Instrumentation (59). Two sampling intervals will be utilized. First, the sampling interval will be 5-minutes for the 15-minute following each successive short bout of exercise in seated position (32, 34). Repeat measurement will be taken during the 15-minute period if the first measurement is unsuccessful. The second sampling interval will be 15±5 minutes (60) for a 12-hour collection period following the all three treatments (1200 to 0000 hours). One repeat measurement will be taken if the first measurement is unsuccessful. The monitor will be programmed to take no readings following 12-hour collection period. The cuff inflation for each measurement will be 30 mm Hg greater than the previous reading, and the cuff deflation will be set at 2 mm Hg·second-1 (7).

Individual blood pressure measurements will be reviewed for missing and erroneous readings. Reading will be purged if 1) data are missing, 2) systolic blood pressure is lower than diastolic pressure, or >240 mm Hg or <50 mm Hg, 3) diastolic blood pressure is >140 mm Hg or < 40 mm Hg, or 4) heart rate is >150 or <40 beats/minute. System tagged data will be eliminated if 1) systolic blood pressures deviate ±50 mm Hg, 2) diastolic blood pressures deviate ±20 mm Hg, or 3) heart rate deviates ±30 beats from the surrounding values. The number of recordings taken and the number of recordings will be reported.

Ambulatory blood pressure data will be analyzed for average systolic and diastolic blood pressure. Blood pressures will be averaged for the 1) 15-minute following the first three short bout of exercise, 2) each hour following the fourth short bout of exercise as well as following one long bout of exercise and control, and 3) the duration of respective blood pressure reduction. The duration of respective blood pressure reduction will be determined by the length of time the hourly blood pressure differs significantly from the control treatment. The magnitude of respective blood pressure reduction will be the average blood pressure reduction for the duration of the blood pressure reduction.

**Power Spectral Analysis of the RR Interval of the Electrocardiogram**

The Aria Digital Recorder (Del Mar Reynolds Medical, Inc., Irvine, CA) will be used to monitor heart rate variability. Subjects will be requested to empty their bladder before beginning each exercise treatment to avoid any increase of sympathetic nerve activity through bladder distension (15). The data from Aria

Digital Recorder will be scanned on a computer-assisted Holter system (Impresario, Solo Holter analysis software, Del Mar Reynolds Medical, Inc., Irvine, CA) for the variables of heart rate variability. Frequency-domain measures of heart rate variability will be assessed using the fast Fourier transform. The manual editing of the R-R interval data will be performed to ensure correct identification and classification of every QRS complex (57). Artifact and ectopic beats will be removed for the R-R interval calculation. The relative number and duration of R-R intervals which are omitted and interpolated will be reported.

The total power will be calculated by the standard deviation of the R-R interval (<0.1 Hz). The spectral analysis of the total 12-hour record will be computed using the whole range of high frequency (0.15 to 0.04 Hz), low frequency (0.04 to 0.15 Hz), and very low frequency (0.003-0.04 Hz) components. Spectral analysis in 12-hour period will be obtained from the average 5-minute segments. The ratio of low frequency to high frequency will be determined. Frequency components will be reported in absolute units (ms2) and normalized units (%). Normalized units represent the relative value of each power component in proportion to the total power minus the very low frequency component (14, 57). Absolute and normalized units will be used in analysis.

**Accelerometer**

The purpose of monitoring physical activity is to statistically control the differences of physical activity in each treatment. The amount of physical activity

will be used as a covariate if there is a significant difference found among the three conditions. An RT3 (Stayhealthy, Inc., Monrovia, CA) will be used for a 12-hour collection period following the all three treatments. The RT3 has been validated for measuring physical activity (52). The RT3 is a battery powered three-dimensional (tri-axial) accelerometer. The RT3 will be firmly attached to a belt on the hip at the anterior axillary line of the dominant leg. RT3 records data in three axis (X, Y, and Z) using three separate accelerometers positioned internally at 90 degrees to one another. It measures motion as acceleration of the body. Output from each accelerometer is reported along with a composite three-dimensional signal called the vector magnitude. The vector magnitude will be used in analysis. RT3 will be programmed to sample data every second and average over one minute (using Mode 3) period for 12-hour.

**Preparation of Subjects**

The blood pressure monitor will be worn on the non-dominant arm. Seven EKG electrodes (three from ambulatory blood pressure monitor and four from Holter monitor) will be placed on the chest. Electrode wires and blood pressure tubing will be taped securely to the chest. RT3 will be worn on the hip at the anterior axillary line of the dominant leg. Subjects will be asked to document the following: 1) time of sleep, 2) time at work, 3) time of meals, and 4) time and type of leisure physical activities. Subjects will be asked to do the similar routines of the activities of daily living on all treatment days. Subjects will be instructed 1) not to exercise, 2) not to take a shower, 3) not to use an electric blanket, 4) not to

operate a lawn mower, a vacuum cleaner or any equipment which causes vibration, 5) replace electrodes with new electrodes when electrodes become loose, and 6) to relax and straighten out the arm during the recording interval for the entire 12-hour period.

### *STATISTICAL METHODS*

The SPSS software (SPSS 12.0) will be used for all statistical analyses. Values will be expressed as means ± standard deviations. Statistical analyses will be performed by use of descriptive statistics, and analysis of variance (ANOVA) for repeated measures. The Tukey test will be used for post hoc comparisons. The significant level will be set at $p<0.05$.

Descriptive statistics will be performed to describe the characteristics of subjects. The variables are sex, age, body mass index (kg/m2), screening systolic and diastolic blood pressures, and $VO_2$peak. One-way ANOVA with repeated measures will be used to test the differences in the amount of physical activity measured by vector magnitude on each treatment.

**The Accumulation of Short Bouts versus One Long Bout of Exercise**

1. The blood pressure reduction following the accumulation of four short bouts of exercise will not be different from the reduction following one long bout of exercise in adults with prehypertension.
    a. In order to determine the duration of blood pressure reduction, two-way ANOVA with repeated measures (Treatments X Time) will be

used. The dependent variables to determine the duration of blood pressure reduction will be average hourly systolic and diastolic blood pressures. In order to determine the difference in the duration of blood pressure reduction, paired T-test (Treatments) will be used. The dependent variables for the difference in the duration of blood pressure reduction will be time (hour).

b. In order to determine the difference in the magnitude of blood pressure reduction, paired T-test will be used. The dependent variables for the difference in the magnitude of blood pressure reduction will be average systolic and diastolic blood pressure for the duration of the blood pressure reduction found in 1-a (mm Hg).

2. The sympathetic modulation, measured by power spectral analysis of the RR interval of the electrocardiogram, will be associated with the blood pressure reduction following the accumulation of short bouts of exercise and one long bout of exercise in adults with prehypertension.

    a. In order to determine the association between the blood pressure reduction and sympathetic modulation, Pearson correlation will be used. The dependent variables will be the magnitude of systolic and diastolic blood pressure reduction and the changes in sympathetic modulation (measured by low and high frequency component as well as the low to high frequency ratio of the power spectral analysis of the RR interval).

3. The association between blood pressure reduction and sympathetic modulation following the accumulation of four short bouts of exercise will not be different from the association following one long bout of exercise in adults with prehypertension.
    a. In order to compare the associations between the magnitude of blood pressure reduction and the change in sympathetic modulation (measured by low and high frequency component as well as the low to high frequency ratio of the power spectral analysis of the RR interval) for each treatment, the test of significance will be performed for r. The dependent variables will be Pearson correlation coefficients (r) between blood pressure reduction and sympathetic activities following both exercise treatments.

**Successive Short Bouts of Exercise**

1. The magnitude of blood pressure reduction following each successive short bout of exercise will be different in adults with prehypertension.
    a. In order to compare the magnitude of blood pressure reduction from baseline following each successive short bout of exercise, one-way ANOVA with repeated measures will be used. The dependent variables will be the 15-minute average systolic and/or diastolic blood pressures following each short bout of exercise.

2. The sympathetic modulation, measured by power spectral analysis of the RR interval of the electrocardiogram, will be different following each successive short bout of exercise in adults with prehypertension.
    a. In order to compare the changes in sympathetic modulation, one-way ANOVA with repeated measures will be used. The dependent variables will be the 15-minute average sympathetic modulation (measured by low and high frequency component as well as the low to high frequency ratio of the power spectral analysis of the RR interval) following each short bout of exercise.

***SIGNIFICANCE***

Hypertension has long been known to be a major modifiable risk factor for cardiovascular disease. Exercise is one of lifestyle modification for the prevention of hypertension. The magnitude and duration of blood pressure reduction from traditional exercise prescription, 20 to 60 minutes of moderate aerobic exercise, is clinically significant in hypertensive individuals. Exercise, however, is one of the greatest barriers among other lifestyle modification to blood pressure control (8). One of the primary barriers to exercise is the lack of time (11, 30, 56). Short bouts of exercise may fit better into a busy schedule than a single long bout (9). Thus, the new exercise prescription, the accumulation of moderate physical activity on most if not all days of the week, has been advocated as a lifestyle modification for the prevention of hypertension.

More investigation is required to determine the magnitude and duration of the new exercise prescription in prehypertension.

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# *VITAE*

## *PERSONAL INFORMATION:*


| | |
|---|---|
| Name: | Saejong Park, Ph.D. |
| Office Address: | Clinical Exercise Physiology Laboratory<br>HPER Building, Room 070<br>Department of Kinesiology<br>School of Health, Physical Education and Recreation<br>Indiana University<br>Bloomington, Indiana 47405<br>U.S.A.<br>Office Phone: (812) 855 – 7556<br>E-mail address: saejpark@indiana.edu |
| Home Address: | 931 Woodbridge Drive<br>Bloomington, IN 47408<br>U.S.A.<br>Home Phone: (812) 334 - 0331 |


## *ACADEMIC BACKGROUND:*

| | |
|---|---|
| Ph.D. | Clinical Exercise Physiology<br>Medical Science Minor<br>Indiana University, Bloomington, IN<br>April 2006 |
| M.S. | Exercise Physiology<br>Indiana University, Bloomington, IN<br>May 2001 |
| B.S. | Chemistry<br>Kyung-Hee University, Seoul Korea<br>February 1996 |

***PROFESSIONAL EXPERIENCE**:*

Lecturer — Indiana University, Bloomington, IN
Department of Kinesiology
2004 - Present

Associate Instructor — Indiana University, Bloomington, IN
Department of Kinesiology
2000 – 2004

Courses Taught as an Associate Instructor and/or Lecturer at the Department of Kinesiology

Exercise Science Classes:

*K561 - Clinical Exercise Physiology Laboratory*
*P409 - Exercise Physiology Laboratory*
*P419 - Fitness Testing and Interpretation*
*P420 – Exercise Leadership and Program Design for Healthy and Special Population*

Physical Education Classes:

*P216 - Current Concepts in Physical Fitness*
*P219 - Weight Control lab*
*E119 - Personal Fitness lab*

Courses Taught as an Associate Instructor at the School of Health, Physical Education and Recreation

Applied Statistics:

*T691 – Correlational Techniques*
*T693 - Experimental Design and Analysis*
*T591 – Interpretation of Data in HPER*
*T592 - Statistical Analysis of Behavioral Data*

Internships/ Clinical Rotation

Bloomington Hospital Cardiac/Pulmonary Rehabilitation (Spring, 2002)
Phase I and II
Cardiovascular Testing

Internal Medicine Association (Summer II, 2001)
Cardiovascular Testing

Bloomington Hospital Cardiac/Pulmonary Rehabilitation (Summer I, 2001)

## *RESEARCH AND CREATIVE ACTIVITY*

*i) FOCUS*

My research interests focus on the exercise prescription for health and disease. I have been investigating the role of the exercise in controlling blood pressure in adults with prehypertension and hypertension. The long-term goal of these projects is to develop short- and long-term intervention programs to prevent and control the cardiovascular disease for these populations. I also have studied force production using mouse skeletal muscle in vitro, and athletic performance.

*ii) REFEREED PUBLICATIONS*

**Park, S.,** Rink, LD, and Wallace, JP (in press) The accumulation of physical activity leads to a greater blood pressure reduction than a single continuous session in prehypertension. *Journal of Hypertension*.

**Park, S.,** Rink, LD, and Wallace, JP (submitted) Accumulation of physical activity: blood pressure reduction between sessions. *Medicine and Science in Sports and Exercise*.

**Park, S.,** Jastremski, CA, and Wallace, JP (2005) Time of day for exercise on blood pressure reduction in dipping and nondipping hypertension. *Journal of Human Hypertension*: 19, 597-605.

Padilla, J., Wallace, J.P., and **Park, S** (2005) The accumulation of physical activity reduces blood pressure in pre- and hypertension. *Medicine and Science in Sports Exercise*: 37, 1264-1275.

Lehmkuhl, L.A.A., **Park, S.,** Zakutansky, D.W., Jastremski, C.A. and Wallace, J.P. (2005) Reproducibility of postexercise ambulatory blood pressure in stage I hypertension. *Journal of Human Hypertension*: 19, 589-595.

Wallace, J.P., **Park, S.,** Zakutansky, D.W., Lehmkuhl, L.A.A. and Jastremski, C.A. (2005) Time of day to monitor ambulatory blood pressure affects outcome. *Blood Pressure Monitoring*: 10, 43-50.

Nagahama, H., Hanna, J.D., **Park, S.**, and Stager, J.M. (2004). Reliability and validity of a field test for determination of onset of blood lactate accumulation in soccer players. *Journal of Training Science for Exercise and Sports*: 16, 227-235.

*iii) PUBLISHED ABSTRACTS AND RESEARCH PRESENTATIONS*

**Park, S.,** Scherzinger, J. R., Bollinger, L. C., Nuseibeh, L. O., Rink, L. D., & Wallace, J. P. (in press). Blood Pressure Reduction in Prehypertension: Accumulation of Physical Activity vs. a Single Continuous Session. *Medicine and Science in Sport and Exercise, 38*(5 Supplement).

**Park, S.,** Collins, K. G., Roble, A. E., Rush, L. S., Zakutansky, D. W., Jastremski, C., et al. (2004). Blood Pressure Response to Exercise in Prehypertensive Adults. *Medicine and Science in Sport and Exercise, 36*(5 Supplement), S251.

Harris, R., Padilla, J., **Park, S.,** & Wallace, J. P. (2004). Blood pressure reduction following physical activity: a case study approach. *Medicine and Science in Sport and Exercise, 36*(5 supplement), S251.
Padilla, J., **Park, S.**, Harris, R., & Wallace, J. P. (2004). Ambulatory Blood Pressure Response Following Free-Living Physical Activity in Pre- and Hypertensive Adults. *Medicine and Science in Sport and Exercise, 36*(5 supplement), S251.

Wallace, J. P., Padilla, J. P., **Park, S. J.,** & Harris, R. A. (2004). What is the adherence to free-living physical activity? *Medicine and Science in Sport and Exercise, 36*(5 Supplement), S64.

Krasnoff, J. B., Wallace, J. P., **Park, S.,** Wallace, J. P., Painter, P. L. & Vardaxis, V.G. (2004). Activation of the rectus abdominis during activities of daily living and therapeutic exercise. *Medicine and Science in Sport and Exercise, 36*(5 supplement), S35.

Zakutansky, D. W., Kitano, K., **Park, S.,** Koceja, D. M., & Wallace, J. P. (2004). Sensory and motor responses to acute ischemia in healthy individuals. *Medicine and Science in Sport and Exercise, 36*(5 supplement), S165.

**Park, S. J.,** Black, K. N., Weaver, V. R., Hawkins, C., Jastremski, C. A., & Wallace, J. P. (2003). Is evening exercise more effective than evening exericse in reducing blood pressure in nocturnal non-dipping hypertension. *Medicine and Science in Sports and Exercise:* 35, S174.

Wallace, J. P., **Park, S.J.,** Lehmkuhl, L. A. A., & Jastremski, C. (2003). Do nocturnal dippers and non-dippers respond similarly to exercise treatment for hypertension? *Medicine and Science in Sports and Exercise*, 35, S174.

Krasnoff, J. B., Raglin, J., Zakutansky, D. W**., Park, S.,** Wallace, J. P., & Painter, P. L. (2003). Predictors of adherence to a home-based exercise program in liver transplant recipients. *Medicine and Science in Sport and Exercise, 35*, S319.

**Park, S.**, Lehmkuhl, L.A.A., Tanner, D.A., Jastremski, C.A., and Wallace, J.P. FACSM (2002). Effects of exercise treatment on ambulatory blood pressure and diurnal variation in nocturnal non-dipping hypertension, Medicine and Science in Sports and Exercise: 34, S12.

Zakutansky, D. W., **Park, S.**, Lehmkuhl, L. A. A., Jastremski, C. A., & Wallace, J. P. (2002). Reproducibility of dipping and non-dipping nocturnal ambulatory systolic blood pressures in borderline hypertensive adults. *Medicine and Science in Sport and Exercise:* 34, S12.

**Park, S.**, Lehmkuhl, L.A.A., Tanner, D.A., and Wallace, J.P. FACSM (2001). Reproducibility of quantifying the circadian blood pressure patterns utilizing cumulative sums in borderline hypertensive adults, Medicine and Science in Sports and Exercise: *33*, S28.

**Park, S.**, and Brechue, W.F., FACSM (2000*).* Changes in calf volume alter plantar flexion torque production, Medicine and Science in Sports and Exercise: 32, S361.
Nagahama, H., Hanna, J.D., **Park, S.**, and Stager, J.M., FACSM (June, 2000). Reliability and validity of a field test for determination of OBLA in soccer players, Medicine and Science in Sports and Exercise: 32, S319.

*vi) EXTRAMULAR FUNDING*

<u>Exercise Intervention in Prehypertension</u>:
Principle investigator: Saejong Park, MS

Blood pressure reduction following the accumulation of physical activity versus one long bout of exercise in prehypertension (2004 & 2005). Doctoral Student Grant-in-Aid, Indiana University, $1,000 [funded]

Accumulation of physical activity versus exercise: blood pressure reduction in prehypertension (2004). Gatorade Sports Science Institute Student Grant-in-Aid ($1,500) [funded]

Exercise Intervention in Hypertension:

Principle investigator: Janet P. Wallace, Ph.D., FACSM

A comparison of a single exercise treatment to a physical activity treatment in hypertension and prehypertension (January 2004). **American Heart Association, $65,980** [not funded]

The influence of time of day for exercise on diurnal blood pressure in dipping and non-dipping hypertension (January 2002). **American Heart Association, $214,354** [not funded]

The influence of time of day for exercise on diurnal blood pressure in dipping and non-dipping hypertension (July 2001). **American Heart Association, $213,637** [not funded]

Exercise Intervention in Diabetes:

Principle investigator: **Janet P. Wallace, Ph.D., FACSM**

Exercise intervention on integrative nerve function in diabetes (January 2001). **National Institute of Health, $1,077,405** [not funded]

Effect of exercise on integrative nerve function in diabetes (April 2000). **National Institute of Health, $1,171,063** [not funded]

*v) RESEARCH AWARDS*

Travel Grant–In–Aid Award (2006) from School of Health, Physical Education & Recreation, Indiana University ($200)

Travel Grant–In–Aid Award (2004) from School of Health, Physical Education & Recreation, Indiana University ($400)

Summer Research Assistance Award (2003) from the Department of Kinesiology, School of Health, Physical Education & Recreation, Indiana University ($1,400)

Travel Grant–In–Aid Award (2003) from School of Health, Physical Education & Recreation, Indiana University ($310)

Summer Research Assistance Award (2002) from the Department of Kinesiology, School of Health, Physical Education & Recreation, Indiana University ($1,400)

Travel Grant–In–Aid Award (2002) from School of Health, Physical Education & Recreation, Indiana University ($200)

Research Grant–In–Aid Award (2001) from School of Health, Physical Education & Recreation, Indiana University ($615)

Travel Grant–In–Aid Award (2001) from School of Health, Physical Education & Recreation, Indiana University ($200)

Research Grant–In–Aid Award (2000) from School of Health, Physical Education & Recreation, Indiana University ($874)

Travel Grant–In–Aid Award (2000) from School of Health, Physical Education & Recreation, Indiana University ($200)

Research Grant–In–Aid Award (1999) from School of Health, Physical Education & Recreation, Indiana University ($200)

The Award of the Excellence for graduate students (1998) from the office of International Programs at Indiana University ($848)

## *PROFESSIONAL AFFILIATIONS*

American College of Sports Medicine (1998 - )
Korean Alliance for Health, Physical Education, Recreation and Dance (2005 - )
Korean Society of Exercise Physiology (2005 - )

## *LICENSE OR CERTIFICATION*

Exercise Specialist – American College of Sports Medicine (2003 - present)
CPR Certification – American Heart Association (2000 - present)
AED Certification – American Heart Association (2001 - present)
First Aid Certification
Science Teaching License for the Secondary School in Korea (1996)